EPA OVERSIGHT ON DIOXIN CONTAMINATION

HEARING

BEFORE THE

SUBCOMMITTEE ON NATURAL RESOURCES,
AGRICULTURE RESEARCH AND ENVIRONMENT

OF THE

COMMITTEE ON
SCIENCE AND TECHNOLOGY
U.S. HOUSE OF REPRESENTATIVES

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EPA OVERSIGHT ON DIOXIN CONTAMINATION

WEDNESDAY, MARCH 23, 1983

House of Representatives,
Committee on Science and Technology,
Subcommittee on Natural Resources, Agriculture
Research and Environment,
Washington, D.C.

The subcommittee met, pursuant to notice, at 1:08 p.m., in room 2318, Rayburn House Office Building, Hon. James H. Scheuer (chairman of the subcommittee) presiding.

Present: Representatives Scheuer, Torricelli, McGrath, Schneider, Chandler, and Lewis.

Staff present: George Kopp, staff director; Jim Greene, science consultant, majority; Mary Beth McJury, minority counsel; and Kim Moses, clerk.

Mr. Scheuer. The Subcommittee on Natural Resources, Agriculture Research and Environment will come to order.

Investigations by the subcommittee staff have lead to the disclosure that Dr. John Hernandez, Acting Administrator of EPA, personally intervened at EPA to allow the Dow Chemical Co. to alter a draft report and supress all references to Dow's responsibility for dioxin contamination in and around its plant in Midland, Mich.

In fact, as a result of Dr. Hernandez' unprecedented intervention, all references to studies showing the adverse health effects of dioxin were removed from that report before it was subject to the peer review process.

Today's hearing will examine the scientific validity of the health data that was eliminated from the report. We will hear testimony from an EPA epidemiologist who proposed a study of birth defects in Midland, Mich., which of course is the site of the Dow Chemical plant.

The proposal indicates that in 1972 and 1973 Midland had three times the rate of birth defects that prevailed in the rest of the State of Michigan. The report also suggested that dioxin from the Dow plant had contaminated the environment in Midland and may—I repeat, may—have led to the birth defects.

Finally, our hearing will explore the extent of dioxin contamination in the Midland area, and we will pay attention to two specific questions:

First, the question of Dow's own data that showed soil contamination at levels ranging from one-third of a part to 100 parts per billion of dioxin.

Second, we will examine recent analyses by EPA scientists which show that fish in the Tittabawassee River, below the Dow plant, had unacceptably high levels of dioxin, approximately twice the acceptable level of dioxin.

Information obtained from today's hearing should indicate the extent of dioxin contamination in Midland, Mich., as well as to point to the additional research and the additional studies that are necessary to insure that the health of the American people is adequately protected.

We have our work cut out for us.

I would now like to recognize the distinguished ranking minority member of the subcommittee, Congressman Ray McGrath of New York.

Mr. McGRATH. Thank you, Mr. Chairman.

I am pleased today to welcome our panels of distinguished guests, who will testify about a very, very important issue which has become a focus of national attention.

In reviewing the testimony for today's hearing, it becomes apparent that what we have is, at very best, a strong disagreement between two groups of scientists. I think it is crucial that we determine the scientific accuracy of these studies relating dioxin to human health problems.

I am hopeful that the testimony we receive today will assist us in determining what additional research and studies are necessary to insure that the health and safety of the American people are protected.

I look forward to receiving the testimony of the witnesses.

Thank you, Mr. Chairman.

Mr. SCHEUER. Thank you, Mr. Ranking Minority Member.

All right. Our first witnesses will be Mr. David Buzzelli, Dr. Robert Bumb, and Dr. Perry Gehring.

Would you please come forward?

Are all four of you going to testify or just Dr. Bumb, Mr. Buzzelli, and Dr. Gehring?

Mr. BUZZELLI. Mr. Bumb, Mr. Gehring, and myself—I am Mr. Buzzelli—will testify. The gentleman at the end of the table——

Mr. SCHEUER. Who is this gentleman here?

Mr. BUZZELLI. That is what I am trying to explain, sir. He is counsel from the Dow Chemical Co. who is head of our environmental law section.

Mr. SCHEUER. All right, then, it is you three gentlemen who will testify?

Mr. BUZZELLI. Yes, sir.

Mr. SCHEUER. Do any of you have any objection to testifying under oath?

Mr. BUZZELLI. No, we do not, sir.

Mr. SCHEUER. OK. Would you please stand up?

Do you hereby swear to tell the truth, the whole truth, and nothing but the truth, so help you God?

Mr. BUZZELLI. I do.

Dr. BUMB. I do.

Dr. GEHRING. I do.

Mr. SCHEUER. Thank you very much. Please sit down.

All right, you are now under oath.

Mr. Buzzelli, why don't you start with your testimony.

The three of you will be testifying?

Mr. BUZZELLI. Yes, sir.

Mr. SCHEUER. I would like you to try to stick to about 8 minutes, which will give us some time. We have four panels this afternoon. We have a very busy schedule.

If you could try to hit the highlights of your testimony in about 7 or 8 minutes, then we will have some time for questions at the end of this panel.

Mr. BUZZELLI. You mean 8 minutes for all of us, not 8——

Mr. SCHEUER. No, no. I mean 7 or 8 minutes apiece. In other words, we will take between 20 and 25 minutes, and then we will have some time for questions.

We have an egg timer up here. When the bell goes off, we will ask you to wind up your sentence.

Mr. BUZZELLI. Yes, sir. We understand.

Mr. SCHEUER. I have found in my political preaching if I cannot make converts in 8 minutes, I had better go on to the next town. OK?

Mr. Buzzelli, let me say that your complete full testimony will be printed in the record. If you would just chat with us informally for 7 or 8 minutes, then we will go through the other two witnesses, and then we will have a chance to ask you all questions.

STATEMENT OF DAVID BUZZELLI, MANAGER OF MANUFACTURING AND ENVIRONMENTAL SERVICES, MICHIGAN DIVISION, THE DOW CHEMICAL CO., MIDLAND MICH., ACCOMPANIED BY DR. PERRY GEHRING AND DR. ROBERT BUMB

Mr. BUZZELLI. Yes, sir. I do have an opening statement, as do both Dr. Bumb and Dr. Gehring, if I may?

Mr. SCHEUER. Yes. Your full statements—all of your statements, if you have more than one—will be printed in full in the record following your oral presentation.

Mr. BUZZELLI. Thank you.

Mr. Chairman and members of the subcommittee, my name is David Buzzelli, manager of manufacturing and environmental services for the Michigan Division of the Dow Chemical Co. located in Midland, Mich. Seated with me are Dr. Perry Gehring and Dr. Robert Bumb.

In my capacity as manager of environmental services, I deal with the issue which really brings Dow before you today. We are appearing here today voluntarily at the request of the subcommittee to answer questions about dioxin studies conducted by our company and others, and to discuss Dow's role in commenting on an EPA report prepared by region V of the EPA.

We welcome the opportunity to appear before you this afternoon and to present scientific and factual information. We hope that our testimony will help provide a perspective and a foundation for the resolution of your concerns.

We share your concerns about dioxin and we recognize their importance to you, to the general public, and to the citizens of our community. We believe these concerns must be addressed promptly and on a scientific basis. The public's need for credible scientific judgments is paramount. We must try to avoid the confusion that already exists in this very complicated and important area of dioxin in the environment.

For most of the past decade, Dow scientists have pioneered the study of dioxin in the environment and its potential effects on man. Many others have joined in this research effort.

We have attempted, on very short notice, to assemble and summarize the key scientific data, which we provided to this subcommittee yesterday. But, you must remember that there are many scientific research reports on dioxins, and a comprehensive summary is just not possible, given the short notice we had. We will, of course, be happy to add anything further that we can to your inquiry.

Before turning to Dr. Gehring and Dr. Bumb, I would like to respond briefly to your request regarding the region V EPA report. I know that you will be hearing later today from Mr. Adamkus and others regarding this report, so I will confine my comments to Dow's limited role.

Mr. Chairman, I believe it is critical that the subcommittee carefully note the sequence of events involved. Dow did not learn of the report's existence until June 13, 1981, when we were called by the Toronto Associated Press for comments on a story quoting from this leaked report. At that time we knew nothing about the existence of the report at all.

We were naturally quite concerned about a quote that was in the news story, and the quote was something like, "Dow has been the primary contributor to contamination of the Tittabawassee River and Saginaw Rivers and Lake Huron."

We were concerned because we were familiar with the growing body of scientific data that has been developed about dioxin since 1978. In our opinion, the recent data did not support that conclusion. We also began immediately to receive many phone calls from the press for comment, even though we had not seen the document.

Consequently, we attempted to obtain some confirmation of the existence of the report from the EPA, since it was already available to the press. Initially, EPA headquarters personnel did not seem to know of the report. But eventually, on June 29, 1981, we did receive what now appears to have been approximately the fourth draft of the report, dated June 18, 1981, several days after the press had reported the story.

It is important to also note that in the draft copy that we received the entire section on conclusions had already been deleted. The draft that we received did contain two or three sentences which were very similar to the Toronto news story.

From last Friday's testimony before Congressman Dingell's committee, it is apparent now that region V and EPA headquarters had already had considerable discussion on the report long before we received the draft.

We were asked by the Washington office of the EPA to make our comments on the report directly to the authors in region V. The draft that we received already had numerous changes and proposed deletions noted on our copy.

Because we had done a great deal of research on dioxin and because the report itself relied heavily on Dow data, we reviewed the document's scientific analysis very carefully. We treated it as though it were a scientific review and, therefore, took precautions immediately to protect its confidentiality within our company.

Regarding the statement that Dow has been the primary contributor to contamination of the Tittabawassee and Saginaw Rivers and Lake Huron, it was our suggestion to region V that we simply change the word from "the EPA 'concludes' " to "the EPA 'speculates'." We felt that this change would be more accurate scientifically, considering the data that had been developed on dioxins since 1978.

Following the telephone conversation between Dr. Kagel, myself, Dr. Clark, and Mr. Kee of region V, we were told that region V would take our comments under advisement and, to the best of my knowledge, that is the last time anybody in Dow Chemical had any contact with the EPA on this report. Apparently, further changes were made to the report following discussions between region V and EPA headquarters in Washington.

Let me reiterate, first, our involvement in this issue was simply an inquiry to the EPA about a leaked report; second, a scientific review of the report; and, third, a telephone call to the author with our comments. I want to emphasize that Dow did not apply any pressure to have the report changed. We simply made our comments to the author and we had no knowledge of the apparently extensive discussions that had previously and subsequently occurred between region V and EPA headquarters.

Thank you for allowing us to clarify our limited role in what has become a very complicated event.

I would like now to turn the microphone over to Dr. Perry Gehring who will make a brief introductory statement.

Dr. GEHRING. My name is Perry Gehring. I currently serve as Dow's vice president for agricultural chemical research and development and also director of health and environmental science. In these positions I have overall responsibility for Dow's environmental health research program.

Today I would like to briefly review the available animal and human data to help you put the health risks of exposure to 2,3,7,8-TCDD, tetrachlorodipenzo-P-dioxin, in perspective. I provided the subcommittee a more detailed statement with supporting scientific citations yesterday.

I am pleased to be here today to discuss Dow's long commitment to the sound use of its products—a program referred to as product stewardship. Because TCDD was a miniscule trace contaminant in a few trichlorophenol-derived products, Dow has conducted 37 health-related studies on TCDD over the past decade, many of which have been published. Much of what we know about the effects of TCDD in animals and in humans is a direct result of this large Dow research effort.

Human data suggest that laboratory animals are more sensitive than man, particularly when one considers the extremely limited exposure of man to the compound. In several industrial accidents where comparatively large amounts of TCDD have been released, animals have died while humans exposed have had only mild effects, primarily chloracne, a unique acne-like condition of the skin usually symmetrical.

Although some of these accidently exposed workers developed other disorders such as liver toxicity, chloracne almost always appeared as a warning sign and was frequently present in the absence of any other symptoms. These and other studies have led the American Medical Association to conclude that without chloracne, the likelihood of significant exposure to, or adverse health consequences from, TCDD is remote.

In our research on the chronic effects of TCDD in laboratory animals we have learned that while at high doses—that is, doses sufficient to cause obvious manifestation of toxicity, including life shortening—laboratory animals will experience reproductive difficulties and some forms of cancer. We have clearly established that lower doses can be tolerated by laboratory animals without observable adverse effects using the most sensitive techniques available.

I want to emphasize that there can be no toxicity without exposure. Toxicity is a function of exposure as well as its capability to produce adverse effects on laboratory animals once inside the body. When humans have been exposed accidently to massive amounts of TCDD which severely poisoned animals, the effects on humans were less severe.

For example, a 1976 accidental explosion in an Italian hexachlorophene plant near Seveso exposed the surrounding population to large amounts of TCDD. While many animals died, Italian authorities and other researchers found that the only clinically definable effects on humans were mild chloracne.

As you have heard, some claim to have found an increase in birth defects in Midland, Mich.—the site of one of Dow's largest chemical manufacturing facilities. The State of Michigan Department of Public Health conducted an investigation and found that the transitory increase for the years 1971 through 1974 was due to increased reporting of minor birth defects. Major birth defect rates remained relatively stable. Before and after this period, rates have been at or below State rates. If birth defects were due to widespread chemical contamination, they should have gone up and stayed up. Our study of Dow workers has revealed no increase.

Claims have also been made that TCDD exposure causes soft tissue sarcomas, a rare family of tumors. In contrast to the Swedish studies indicating an increased incidence of soft tissue sarcomas in those exposed to phenoxy herbicides, studies in New Zealand, and elsewhere in fact, failed to identify a single case of soft tissue sarcoma among licensed herbicide applicators. Occupations associated with the use of phenoxy herbicides and chlorophenols demonstrated no marked propensity for developing this rare tumor in a study conducted in the State of Washington. In this study the two occupations at highest apparent risk of developing soft tissue sarcomas were marine engineers and bankers.

Nor do the epidemiology studies support the theory that dioxin is a potent carcinogen. An investigation of workers exposed during a 1949 industrial accident demonstrated no increase in mortality due to cancer. More recently, a study of over 8,000 employees of our Midland, Mich., facility concluded their overall mortality was about 20 percent less than expected when compared to the experience of the United States population, and their overall cancer mortality was 5 percent less than expected.

In summary, while highly toxic in certain animal test systems, TCDD's hazard to humans, which is a function of not only inherent toxity but exposure level as well, has been overemphasized. In the absence of chloracne, there is no clear evidence that TCDD poses any risk to human health, either acutely or chronically.

This is not to say that we should ignore exposure to TCDD. Contamination which constitutes a hazard to man should be corrected, but exposure to nonhazardous levels of TCDD cannot be eliminated.

Thank you.

[The prepared statement of Dr. Gehring follows:]

TESTIMONY ON TCDD AND HEALTH CONSIDERATIONS: AN OVERVIEW
TCDD AND HEALTH CONSIDERATIONS
TOXICITY OF 2,3,7,8-TETRACHLORODIPENZO-P-DIOXIN (TCDD)

BY

DR. PERRY J. GEHRING

BEFORE THE

SUBCOMMITTEE ON NATURAL RESOURCES
AGRICULTURE RESEARCH AND ENVIRONMENT

COMMITTEE ON SCIENCE AND TECHNOLOGY

HOUSE OF REPRESENTATIVES

ON MARCH 23, 1983

TCDD AND HEALTH CONSIDERATIONS: AN OVERVIEW

The toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) has been comprehensively examined in multiple acute, subacute and chronic animal studies. Extensive research has been conducted to determine its sources and its environmental fate. Human populations inadvertently exposed to varying levels of TCDD in both industrial and community settings have been investigated. While overall assessment of this extensive data base indicates that TCDD has widespread environmental distribtution, the animal data indicate the current levels in the environment do not constitute a significant risk. This is a conservative assessment since comparisons of human and animal data consistently suggest humans are less sensitive.

TCDD is produced during the normal burning of wood, fossil fuels, and municipal wastes as well as occurring as a byproduct in the manufacturing of certain chemicals. TCDD breaks down rapidly in sunlight, and binds readily and with high affinity to soils. This latter property makes TCDD resistant to leaching and greatly reduces the hazard to animals and people by diminishing the amount of TCDD available for absorption from the skin or gastrointestinal system.

Acute animal toxicity studies have shown marked species differences, with up to a 5,000-fold differential between the single oral LD_{50}* dose for the guinea pig and hamster. The findings at Seveso, Italy reinforce this species differential. In that case environmental contamination was sufficient to kill a number of wild and domestic animals, but no serious human illness occurred as a result of exposure.

Lifetime animal toxicity and three-generation reproduction studies have clearly established doses which can be tolerated without adverse toxic or reproductive effects. Tumor induction in animals was associated only with lifetime ingestion of higher doses of TCDD which also produced substantial systemic toxicity, characterized by obvious pathological changes in tissues, abnormal clinical chemistry values, marked weight loss and decreased longevity. The animal studies have consistently shown that signs of lesser toxicity (e.g. liver toxicity) clearly precede the more serious toxic effects (e.g., carcinogenesis, teratogenesis and embryo/fetotoxicity). There appear to be no definitive in vivo correlates of mutagenicity in higher animals or man. Human cytogenetic evaluation of maternal blood and fetal tissues at Seveso indicated no mutagenic effects related to TCDD.

TCDD is capable of causing an acnegenic response, referred to as chloracne, in man and a similar skin response in certain animals. This condition is considered the hallmark of human overexposure to TCDD. It is generally felt that human toxicity does not occur without prior or concomitant chloracne.

*LD_{50} or Lethal Dose 50 is the estimated dose level at which 50% of the exposed animals die.

In Seveso, Italy, where over 30,000 people were exposed, there were 100-200 cases of chloracne. The only other clinical symptoms described were transient gastrointestinal and mild nerve disorder which subsided after exposure was reduced.

In addition, no effects on the health of pregnant women, no teratogenic or adverse effects on fertility were noted. Nor were there any consistent pathogenic effects on the course of the pregnancies that could be attributed to the dioxin exposure. Unfortunately, the related panic did lead to a number of medically induced abortions. Examination of these conception products revealed no evidence of injury attributable to TCDD.

Recently some allegations have been made that transient increases in birth defects in Midland, Michigan (the site of one of Dow's largest chemical manufacturing facilities) are due to environmental contamination by dioxin. In 1976, the State of Michigan Department of Health conducted an investigation of this matter. They concluded that the transitory increase for the years 1971 through 1974 were attributed to the increased reporting of minor birth defects. The major birth defect rates remained relatively stable. Rates before and after this period have been at or below state rates. If birth defects were due to widespread chemical contamination, they should have gone up and stayed up. They did not.

TCDD is considered to be carcinogenic in animals via a nongenetic promotional mechanism, but only at levels associated with substantial toxicity in the test animals. Furthermore, the types of tumors found in animals do not support the theories that TCDD is the cause of soft tissue sarcomas. Nor do the most recent epidemiology studies support a cause-effect relationship. Bulk quantities of phenoxyacetic acid herbicides thought to have trace quantities of TCDD have been used in New Zealand since the 1940's, yet a recent case-control study failed to identify a single case of soft tissue sarcoma among licensed herbicide applicators. In Washington State, the two occupations at highest apparent risk of developing soft tissue sarcomas were marine engineers and bankers. Occupations associated with the use of phenoxyacetic acid herbicides and chlorophenols demonstrated no marked propensity for developing this rare type of cancer.

Nor do the epidemiology studies support the theory that dioxin is a potent multiple-site carcinogen. An investigation of workers exposed during a 1949 industrial accident demonstrated no increase in mortality due to cancer. More recently, a study of over 8000 employees of our Midland, Michigan facility concluded their overall mortality was about 20% less than expected when compared to the experience of the United States population and their overall cancer mortality was 5% less than expected.

In summary, 2,3,7,8-tetrachlorodibenzo-p-dioxin is found widely in our environment. While highly toxic in certain animal test systems, its hazard to humans has been overemphasized. In the absence of chloracne, there is no clear evidence that it poses any risk to human health, either short or long term.

TCDD AND HEALTH CONSIDERATIONS

Dow publicly reported a number of years ago that dioxin could be found in the soil of the community surrounding its Midland plant. These levels were similar to those found in other industrialized urban areas. Dow also publicly reported that the dioxin levels were higher in the soil inside the plant. Available data indicate no health risk to either the occupational or the community population.

The following is not an exhaustive review of the literature, but is intended as a brief overview of some key issues that have recently surfaced.

Section A presents data from a 25-year study of Dow employees who worked at the Midland plant. Their overall mortality was almost 20% less than that expected from national experience, and their overall cancer mortality was 5% less than expected. These findings indicate that occupational exposures to chemicals at the Midland location of Dow have not increased general mortality or overall cancer mortality. Indeed, it is reasonable to advocate that working for Dow has had a positive impact on health.

Section B discusses birth defects, more specifically, birth defects in Midland County, Michigan. The data are not consistent with the allegation of adverse reproductive effects due to widespread contamination by a toxic chemical.

Section C addresses the hypothesis that dioxin is a cause of soft tissue sarcomas, a rare form of cancer. Neither the animal toxicology nor the more recent human epidemiology support this theory.

SECTION A: DOW MORTALITY STUDY

In 1976, a research study was published that summarized the mortality experience of over 8,000 men employed by The Dow Chemical Company. The population of interest was defined based on a March 1, 1954 employee census prepared for the Midland, Michigan location of the company; details concerning the cohort definition have been described previously (Ott et al, 1976).

The objective of that initial study was to develop background mortality data on the Dow population, so that findings obtained from smaller studies directed at more specific questions (e.g., questions regarding particular chemical exposures or processes), could be placed in perspective. The observation period for mortality follow-up was 1954 through 1972 and comparisons were to the mortality experience of the corresponding United States white male population. At that time, mortality among Dow employees was found to compare favorably with that of the general United States population.

The objectives of the most recent update of this group of 8,181 employees were to extend the observation period through 1978, and to include comparisons with a community-based group of employed men not engaged in chemical manufacturing activities. In addition, the effects of cigarette smoking on mortality were investigated.

The Dow group consisted of personnel from research departments, the corporate headquarters, and a major manufacturing division of the company. It has been estimated that as many as 500 distinct chemical processes ranging from small batch operations to large continuous and highly automated production units have been onstream at the Midland manufacturing site, including production of trichlorophenol and related products (Ott et al, 1975).

Over 21% of the Dow employees had been hired by the company prior to 1940. Approximately 46% of the men were hired during the 1940's, with the remainder being hired during the early 1950's. For the most part, the men in the study represent long-term company employees. From Table 1 it can be seen that nearly 70% of the men had in excess of 25 years service with the company. This follows, in part, from the manner in which the study population was chosen; that is, a one-time census would favor inclusion of longer-term employees relative to the ever-employed population.

A summary of the vital and employment status of the Dow group through 12/31/78 is given in Table 2. For employees who left the company, vital status was traced primarily through the Social Security Administration. Vital status was known for all but 143 employees (1.7 percent of the total group), most of whom were under 35 years of age at company termination. They contributed no person-years to the calculation of expected deaths after their company termination date. The small percentage of men that were not followed to the end of the study reflects the stability of the workforce at this company location as well as the cohort selection procedure.

Cause of death information was obtained from death certificates for all but nine of the 1,932 deceased members of the study population. A comparison of overall and cause-specific mortality experience of the Dow group with that of the general United States population is provided in Table 3. The comparisons are based on indirect standardization of age- and era-specific (5-year interval) death rates.

Overall mortality in the Dow group was 19% less than that expected for the corresponding United States population. Expressed in another way, life expectancy at age 25 was 73.1 years for the total Dow group, whereas, for the United States white male population, life expectancy in 1972 was 70.9 years. The 2.2 years difference in life expectancy roughly corresponds to the 19% fewer deaths observed over the 24-year follow-up interval.

Cause-specific mortality was also examined for the total Dow group in Table 3. For major cause of death categories, fewer deaths were observed than expected in all categories save one, Benign and Unspecified Neoplasms. There were no statistical findings ($p < .05$) of excess mortality among Dow employees for any cause of death category including 12 subcategories within the Malignant Neoplasms. For Total

Malignant Neoplasms, there were 5% fewer deaths observed than expected based on the United States white male population. Significantly fewer observed than expected deaths ($p < .05$) were seen for Infectious and Parasitic Diseases, Diseases of the Circulatory System, Diseases of the Respiratory System, Diseases of the Digestive System, Symptoms, Senility and Ill-Defined Conditions, All External Causes, and Residual Causes. The very low SMR for Symptoms, Senility and Ill-Defined Conditions follows the geographic pattern of low mortality for this category in the state of Michigan. This pattern is particularly evident in mid-Michigan and is probably a reflection of better than average death certification practices in the pertinent communities.

The finding of favorable mortality in an employee population relative to the corresponding national population is often anticipated in occupational studies and has been referred to as the "healthy worker" effect. At the outset, an initial favorable selection may exist because the general population includes institutionalized and other persons both unavailable for work and less healthy than the average employed person. This selection is thought to vary by disease and to disappear after a period of time. The "healthy worker" effect is of little consequence when cancer is being considered.

The most direct way of neutralizing the selection effects due to employability is to examine mortality in the Dow group relative to that of a comparable employee population not engaged in the manufacture of chemicals. A suitable reference population of employed men was available for comparison purposes because of the prior existence of a community-based prospective health study in another Michigan community. It was possible to identify a subset of men in this community who were employed based on initial interview data and to follow the mortality experience of these men over approximately the same time span as that covered by the Dow study. The employed men in the community-based group represent a cross-section of all occupations in the community but included few, if any, men working in a chemical production facility.

The mortality comparisons between the two employee groups are summarized in Table 4. The conditional risk estimator compares the mortality ratios between the two groups after adjustment for socioeconomic status, age at entry and interval since entry to study. Overall mortality risk was about 10% lower in the Dow than the corresponding non-Dow employee group. Both groups experienced fewer observed than expected deaths based on comparison to the United States white male population. The only statistical differences observed were relative decreases among the Dow population in overall mortality and for Diseases of the Respiratory System.

Cigarette smoking is well recognized as a major determinant of mortality. Although it was not possible to obtain smoking history information on all Dow employees in the present study, routine collection of medical surveillance information included a smoking questionnaire beginning in 1968 that enabled an examination of the relationship between smoking and mortality in a subset of the Dow employees.

A summary of the distribution of smoking habits among Dow employees is given in Table 5. It reveals the expected patterns of higher mortality with increased cigarette smoking. A comparison of the risks associated with smoking in the Dow group and the non-Dow employee group found no evidence of differences between the groups. That is, there was no evidence that general chemical exposure in a chemical manufacturing setting together with cigarette smoking led to any different effects than would be expected for cigarette smoking alone.

Much public concern has been expressed regarding possible adverse health effects of chemicals in the work environment and in the general environment. While there is a broad awareness that most, if not all, chemicals are toxic when sufficiently large doses are encountered, it is not well appreciated that much lower exposures may be tolerated without adverse health effects or observably increased risk.

The findings of the Ott (1983) study may help to provide perspective on this issue. The study results indicate that people can work safely with known toxic chemicals provided proper precautions are taken. The Dow Chemical Company has had an active toxicology program since the 1930's, a formal industrial hygiene program that predated the 1950's, and a long-standing medical surveillance program all geared to the prevention of occupational disease. The present study reflects positively on the adequacy of those programs as well as the health experience of those employed at Dow. It is through understanding the toxicity of chemicals coupled with the prevention of over-exposure that adverse health effects may be avoided.

SECTION B: BIRTH DEFECTS

About five years ago it was reported that the birth defect rates in Midland County were 3-fold above those of the State of Michigan. Midland County is the site of one of Dow's major chemical production facilities. At that time, the State of Michigan Department of Public Health explored the issue. They found an increase had occurred between 1971 and 1974 due to additional reporting of minor congenital malformations. Before 1971 and after 1974, the birth defect rates were at or below state rates. If widespread chemical contamination of the environment was responsible for birth defects, the rates should have gone up and stayed up. They did not.

The data on this transient elevation in birth defects was recently reintroduced by a small local environmental group. While they presented no new data, media reports raised a new wave of concern by giving the impression that the rates were still elevated. The State Department of Public Health is re-exploring the issue and analyzing data from recent years. Their report should be available shortly. In the meantime, the following is a compilation of the data from Dow's files which we had previously obtained from the State of Michigan. All of it is public information. It is government data available to anyone for the asking.

It is very important to note that the absolute numbers of county births and birth defects were small and, thus, rates calculated from them tended to be more variable from year-to-year than the comparable state rates. Table 6 presents the absolute number of events and the total congenital malformation rates from 1965 through 1977 for both state and county. It also breaks the total congenital malformations for the county down into major and minor for the period 1970 through 1975. Given the small number of events in each year, it's obvious the major congenital malformation rates were relatively stable during the entire period. Only the rates for minor congenital malformations varied widely. According to definitions used by state public health officials, major congenital malformations include such things as cleft lip, cleft palate, club feet, dislocated hip, cyanotic heart disease, hydrocephaly, microcephaly and Down's Syndrome. Minor congenital malformations include such things as hydrocele, undescended testicle, and grade I or II heart murmurs without cyanosis, conditions that often go unreported.

In 1982 Dow scientists published a report of a survey of reproductive events among wives of Dow Michigan Division employees exposed to dioxins (Townsend et al, 1982). They analyzed the associations between exposure and spontaneous abortions, stillbirths, infant deaths, and several categories of congenital malformations before and after controlling for multiple confounders independently and in various combinations. They did trend analysis to determine if duration of paternal exposure was related to adverse pregnancy outcome. There were no associations between any exposure and adverse pregnancy outcomes. These findings have recently been confirmed by a study in Australia (Armstrong, 1983).

The most well-known and widely studied incident of community exposure to TCDD followed the July 10, 1976 explosion at the ICMESA trichlorophenol plant at Seveso, Italy. As a result of that accident, approximately seven square miles of the countryside were contaminated by TCDD and other chemicals, exposing as many as 30,000 people to a greater or lesser extent (Homberger et al, 1979; Pocchiari et al, 1979). The heaviest contamination involved an area of 180 acres (Zone A), occupied by 736 people. TCDD was reportedly detected on soil at levels in excess of 15,000 parts-per-billion (ppb) (Fanelli et al, 1982; Homberger et al, 1979). In general, little effect was noted on plant life, but wild animals did die, particularly in zone A. About 4% of the domestic animals in contaminated zones died spontaneously and virtually all these were small animals. When the nature of the contamination was realized after about 9 days, approximately 80,000 domestic animals were slaughtered to prevent their entry into the human food chain (Homberger et al, 1979).

Chloracne, which has generally been regarded as the hallmark or sentinel sign of TCDD overexposure (Crow, 1978) was observed in this population, although at generally low rates, and primarily in children (Caramaschi et al, 1981; Fara et al, 1980; Homberger et al, 1979; Pocchiari et al, 1979). The highest incidence of chloracne reported was about 13-14% among elementary school children in Seveso, and this was generally mild and rapidly resolved in most affected individuals (Homberger et al, 1979; Pocchiari et al, 1979; Reggiani, 1979). Other than chloracne (of which there were ultimately 100-200 cases), nausea, vomiting, itching and headache were the most commonly observed symptoms readily attributable to TCDD exposure (Pocchiari et al, 1979). Headache and gastroenteritis were more commonly noted in individuals with chloracne (Caramaschi, 1981; Pocchiari et al, 1979).

Bisanti et al (1979) concluded that no "major event" had taken place with respect to birth defects, abortions, births and deaths. While this seems to be the consensus, changes in birth defect reporting patterns and in the reporting of "spontaneous" (sometimes "therapeutic") abortions has obscured any small changes which might have occurred (Basso et al, 1980; Homberger et al, 1979; Pocchiari et al, 1979; Reggiani, 1977; Reggiani, 1979). Data on reproductive outcome are scant, and confounded, but Reggiani (1977) reports that examination of conception products in 34 cases of induced abortion revealed no evidence of injury attributable to TCDD; otherwise, pregnancy outcome in the years following 1976 is apparently consistent with Western experience (Pocchiari et al, 1979). Of particular interest, no birth defects were observed during 1977 among the only four births in zone A and among the 66 zone B births. Only those pregnancies coming to term after January 1977 would have been relevant, i.e., those in which July 1976 maternal exposure would have taken place during organogenesis.

Mary things are known to cause birth defects in humans: viral infections, genetic predisposition, smoking, alcohol, and even medications, including excess quantities of certain vitamins. The evidence does not support the inclusion of dioxin on this list. It's important to note that the levels of contamination in Seveso were tens to hundreds of thousands of times greater than in the community of Midland, and there was no increase of birth defects in Seveso.

SECTION C: SOFT TISSUE SARCOMAS

Over the past few years a number of theories have been put forth concerning the human health effects associated with exposures to dioxins. Most of these have been discounted by the growing body of data. Dioxin does not appear to be as hazardous to humans as we initially suspected.

The most persistent theory deals with the possible causal association between 2,3,7,8-TCDD and soft tissue sarcomas. This hypothesis derives from the work of Dr. Hardell and his associates in Sweden (Hardell et al, 1977; Cook, 1981).

But one has to exercise caution against overinterpreting Hardell's current data. It leads to more sophisticated questions, but it does not provide any definitive answers. His reports are too incomplete, both individually and in aggregate, to currently formulate a clear picture of the possible associations between TCDD and soft tissue sarcomas. By analogy, we are in the process of fitting together the pieces of a large jig-saw puzzle. Some of the pieces on the table may be superfluous, false leads that waste time and resources. Other pieces are, and maybe always will be missing; but with each new bit of research, a more complete picture is emerging about whether or not TCDD has major human health implications and, if it does, at what level and for which disease. This process is not unique to TCDD; it is the process of epidemiology (Hammond, 1983; West, 1983). It is the process by which the true causes of human disease are discovered and appropriate preventive measures are instituted. Unfortunately, it is often a complicated and sometimes confusing process.

Hajdu pointed out in a recent review article that soft tissue sarcoma is a generic term for a heterogeneous group of lesions that include more than 100 tumors (Hajdu, 1981). And there are at least 50 reactive lesions that resemble soft tissue neoplasms. The nomenclature of these growths is in flux; and the tumors are so rare that few pathologists have been able to achieve a high degree of expertise and consistency in the diagnosis of specific neoplasms (Patterson, 1978). To date, no single pathologist has reviewed all the histopathological specimens. To date, it is not known whether we are dealing with a single predominant clinical entity or a multitude of diseases. The former would argue for cause and effect. The latter would argue against it. One of the reasons vinyl chloride is accepted as a human carcinogen is the specificity of effect. At high levels, it produces a single type of soft tissue sarcoma: angiosarcoma. It does not produce a general increase of all soft tissue sarcomas.

The common exposure link between various reports of soft tissue sarcomas in occupational groups is 2,3,7,8-tetrachlorodibenzo-dioxin, one of the most toxic chemicals known to man. But is it the real common link? The rigor of exposure documentation varies from study-to-study. In some, based on detailed technical knowledge of the chemical process, analyses of reaction contaminants, and clinical evidence of excessive group exposure, e.g., chloracne, there is strong evidence that 2,3,7,8-TCDD is at least one of the common exposure links. In other reports, the evidence is more presumptive, and in some totally lacking.

Epidemiologists from Monsanto and Dow have reported on the soft tissue sarcoma cases occurring in their occupational cohorts exposed to high levels of 2,3,7,8-TCDD (Zack and Suskind, 1980; Cook, Townsend and Ott, 1980; Zack and Gaffey, 1980). These three were later reviewed by Honchar and Halperin (1981). It is now known there are four cases, three deceased and one still living (Cook, 1981). Table 7 provides an update on those four. There are two new bits of information: case number 3 also had trichlorophenol process exposures and also had chloracne.

Notice the patterns of year of birth, process, chloracne, and cigarettes. Are some of these important, or are they "red herrings"? It is not known yet. These questions will have to be explored in future epidemiological studies. Parenthetically, there have been no cases of soft tissue sarcoma in a cohort of Dow 2,4,5-T employees, none of whom had chloracne (Ott, Holder and Olson, 1980). Nor has there been any soft tissue sarcoma cases reported in the BASF cohort (Thiess, Frentzel-Beyme and Link, 1982). Members of the BASF cohort were exposed to 2,3,7,8-TCDD during a 1953 accident in a trichlorophenol production unit or during cleanup and repair following the accident. Exposures were heavy. Many developed severe chloracne.

The work of Dr. Hardell uses a different type of methodology, the case-control approach, and reports on different patterns and levels of exposure (Hardell and Sandstrom, 1979; Eriksson, Berg, Hardell, Moller and Axelson, 1979). In his first study, he reported a 5 to 6-fold increased risk for those presumptively exposed to phenoxyacetic acids, predominately 2,4,5-T, and chlorophenols; presumptively because the exposure information was subjectively reported by the study participants and/or next of kin. Objective records were incomplete and difficult to interpret. In the second study, he also estimated the risk associated with exposure to phenoxy acids not contaminated with TCDD and found the same magnitude of risk.

Epidemiologists reviewing the information find this confusing. The justification for combining chlorophenols and 2,4,5-T was their commonality of contaminants, TCDD (Erikssson, Berg, Hardell et al, 1979). If that be the case, then phenoxy acetic acids without these contaminants shouldn't have demonstrated an increased risk.

In both of his studies, Dr. Hardell first administered mail questionnaires and then followed up with telephone interviews on a selected subset of subjects. While the questionnaire was designed with the idea of masking the intent of the investigation, the telephone inquiry zeroed in specifically on the exposures of interest: phenoxy acetic acids and chlorophenols.

Interestingly, in his second study the frequency of the various exposures among both cases and controls was reported and most of the risk estimates were elevated. Here they are broken down by whether they were achieved with data from the questionnaire alone or telephone supplement (Table 8). Note that only one, sodium chlorate, is not elevated. Notice also that nicotine has a risk of 6.1. Unfortunately, the risk estimates on the upper agents derived from the questionnaire alone are not known, nor is it known what the risk estimates would have been on the lower agents, given they had been probed in the same depth as were the phenoxies and chlorophenols.

There are at least five alternate interpretations of Table 8. One, exposure to phenoxyacetic acids, chlorophenols and their contaminants may cause soft tissue sarcomas and the elevated risks of all other agents are unimportant. Two, there was recall bias. Those with disease ruminated about their previous exposures and overreported relative to the nondiseased controls. Three, there was observer bias. Those who conducted the telephone interviews knew the underlying hypothesis of the study AND knew who were cases and who were controls. Upon review of the actual questionnaire and the data collection methods, epidemiologists believe both of these conditions were possible. Four, there was confounding. That is, other causes of the sarcomas were not adequately controlled in design or analysis. Ionizing radiation, trauma, foreign bodies, viral infections, genetic predisposition and even materials used by diagnostic radiologists have all been associated with soft tissue sarcomas. None were addressed in Hardell's work. Or, five, phenoxies and chlorophenols are only indirectly associated with the disease. They and all of the agents listed are surrogates for particular types of occupations in which the true cause is found. It will not be known which of the above is or are correct without further research.

Fortunately, this research is going on and the answers are starting to come in. They do not support Hardell's hypothesis concerning soft tissue sarcoma.

Smith and associates (1982) are conducting a case-control study in New Zealand which is designed to avoid some of the apparent data collection flaws of Hardell's work. Herbicide spraying is a registered profession in New Zealand and phenoxyacetic acids have been used in bulk since the late 1940's. In a preliminary report presented at the 1982 International Symposium on Chlorinated Dioxins and Related Compounds, Smith noted he was unable to establish an association between the use of the herbicide and soft tissue sarcoma. In fact, not one of the soft tissue sarcoma patients had ever worked as a licensed phenoxyacetic acid herbicide sprayer.

Milham (1982) explored this issue in the State of Washington using death certificates. While there has been considerable exposure over the years to phenoxyacetic acids and chlorophenols in Washington State, occupations related to their use did not show unusual patterns of death due to soft tissue sarcomas. Surprisingly, the two occupations with the highest proportional mortality ratios were marine engineers and bankers.

Among the deaths in the U.S. Air Force "Ranch Hand" Study, none were due to soft tissue sarcomas (Chesney, 1982). In the BASF cohort of employees heavily exposed to 2,3,7,8-TCDD, there have been no deaths due to soft tissue sarcomas (Thiess et al, 1982). Riihimaki studied Finnish herbicide applicators and found no soft tissue sarcomas (Riihimaki et al, 1982).

Closer to home, the State of Michigan Department of Public Health is investigating the relationship between connective tissue cancer deaths in Midland County and dioxins. They are finding none (Midland Daily News, 1982).

Further research is going on in the United States and elsewhere. The results of these studies should add still further perspective to this whole issue; but right now, the preponderance of evidence is leading us away from 2,3,7,8-TCDD as being a cause of soft tissue sarcomas.

In summary, important information continues to accumulate. For those charged with making administrative decisions from this data, the speed with which it is collected must seem agonizingly slow. For those exposed to these agents and frightened by the premature declarations of cause and effect, the apparent indecision of the scientific community must be frustrating. Nonetheless, efforts must continue to methodically collect the data, analyze it, subject the reports to peer review, refine the hypotheses, and retest them on independent groups of subjects. Only then will it be known whether 2,4,5-T, or chlorophenols, or 2,3,7,8-TCDD cause specific types of diseases; and, if they do, at what levels and under what conditions. The current body of evidence suggests that the only consistent sequelae of TCDD exposure is chloracne. And this is only found at levels of contamination many orders of magnitude greater than those to which the general public may be exposed.

TABLE 1

NUMBER OF DOW MICHIGAN DIVISION EMPLOYEES BY TOTAL LENGTH OF SERVICE WITH THE COMPANY

	Number of Men	Percent
Total	8,181	-----
<1 Year	16	0.2%
1 - 4 Years	256	3.1%
5 - 9 Years	283	3.5%
10 - 14 Years	405	5.0%
15 - 24 Years	1,522	18.6%
25+ Years	5,699	69.7%

TABLE 2

VITAL AND EMPLOYMENT STATUS
OF THE DOW STUDY GROUP
AS OF 12/31/78

	Number	Percent
TOTAL COHORT	8,181	-----
Still Working	2,778	34.0%
Retired and Living	2,622	32.1%
Deceased (Company Records)	1,808	22.1%
LEFT EMPLOYEES		
Deceased	124	1.5%
Known Alive	706	8.6%
Vital Status Unknown	143	1.7%

TABLE 3

OBSERVED AND EXPECTED DEATHS BY CAUSE AMONG 8,181 DOW MICHIGAN DIVISION MALE EMPLOYEES, 1954-1978

(Deaths coded by Revision of ICD in force at the time of death)

Cause of Death Category	Observed Deaths	Expected Deaths[a]	SMR[b]	95% C.L.[c]
All Causes	1932	2379.2	81	78 - 85
Infectious and Parasitic Diseases	13	25.7	51	27 - 86
Malignant Neoplasms, Total	460	482.1	95	87 - 105
Benign and Unspecified Neoplasms	10	6.3	158	76 - 292
Endocrine Nutritional and Metabolic Diseases	37	40.2	92	65 - 127
Diseases of the Circulatory System	1068	1256.3	85	80 - 90
Diseases of the Respiratory System	90	140.3	64	52 - 79
Diseases of the Digestive System	66	121.2	55	42 - 69
Symptoms, Senility and Ill-Defined Conditions	4	27.0	15	04 - 38
All External Causes	136	204.0	67	56 - 79
Residual Causes	39	76.1	51	36 - 70
Unable to Locate Death Certificates	9	----	--	

[a] Expected deaths based on United States white male mortality.

[b] SMR is the standardized mortality ratio and represents the ratio of observed to expected deaths multiplied by 100.

[c] 95% Confidence limits based on Fisher exact limits when observed deaths were less than 20 and approximate limits otherwise.

TABLE 4

OBSERVED AND EXPECTED DEATHS AND CONDITIONAL RISK RATIOS BY CAUSE OF DEATH AND STUDY GROUP, (Dow and Non-Dow Community Based), 1954-1978

(Deaths coded by Eighth Revision of ICD)[a]

Cause of Death Category	Dow Obs/Exp	Non-Dow Community-Based Obs/Exp	Conditional Risk[b]	
			Dow/Com	p-Value[c]
All Causes	1932/2379.2	357/400.4	.90	.044
Infective and Parasitic Diseases	11/ 25.7	1/ 3.4	1.21	.853
Malignant Neoplasms, Total	461/ 482.1	86/ 82.9	.93	.536
Benign and Unspecified Neoplasms	10/ 6.3	2/ 1.0	1.49	.577
Endocrine, Nutritional and Metabolic Diseases	35/ 40.2	8/ 6.9	.89	.752
Diseases of the Circulatory System	1073/1256.3	185/206.7	.92	.245
Diseases of the Respiratory System	92/ 140.3	28/ 23.6	.53	.001
Diseases of the Digestive System	65/ 121.2	13/ 20.9	.72	.252
Symptoms, Senility and Ill-Defined Conditions	4/ 27.0	1/ 4.8	.72	.758
All External Causes	135/ 204.0	23/ 37.3	1.10	.654
Residual Causes	37/ 76.1	10/ 12.7	.72	.321
Unable to Locate Death Certificate	9/ -----	-/ ----	---	-----

[a] For comparability with the community-based study group, it was necessary to recode all deaths to the eighth revision of the ICD. This resulted in minor differences in the observed cause of death distribution from the coding based on revision in force at the time of death.

[b] Conditioned on fixing the expected deaths to equal observed deaths for each stratum formed by socioeconomic status, age at entry and interval since entry category.

[c] Probability of obtaining the observed risk ratios given the null hypothesis of no differences between the two employee groups.

TABLE 5

OBSERVED AND EXPECTED DEATHS BY CIGARETTE SMOKING CATEGORY DOW GROUP

			CAUSE OF DEATH CATEGORY					
			Malignant Neoplasms*					
Cigarette Smoking Category	ALL CAUSES		TOTAL		RESPIRATORY		ISCHEMIC HEART DISEASE	
	Obs/Exp	SMR	Obs/Exp	SMR	Obs/Exp	SMR	Obs/Exp	SMR
Never Smoked	47/111.6	42	10/25.9	39	1/10.4	10	21/43.8	48
Former Smoker	137/225.0	61	36/52.0	69	14/20.8	67	67/88.3	76
Current Smokers								
≤ 1 pk/day	97/114.2	85	27/26.3	103	6/10.5	57	46/43.7	105
> 1 pk/day	55/ 46.9	117	20/10.7	187	11/ 4.3	256	21/18.1	116

*Observed to expected deaths presented as absolute events and as a standardized mortality ratio (SMR).

TABLE 6

CONGENITAL MALFORMATIONS - TOTAL, MAJOR AND MINOR AND RATES -- BY STATE (MICHIGAN) AND COUNTY (MIDLAND), 1965-1977

Year	Congenital Malformations[1]		Total CM Rate[2]		Major CM[3] County		Major CM[4] County	
	State	County	State	County	Number	Rates	Number	Rate
1965	1920	13	1.2	1.1				
1966	1863	13	1.1	1.1				
1967	1750	14	1.1	1.1				
1968	1667	12	1.0	1.0				
1969	1559	9	0.9	0.6				
1970	1515	12	0.9	0.9	9	0.7	3	0.2
1971	1568	29	1.0	2.3	13	1.0	16	1.3
1972	1430	34	1.0	3.2	12	1.1	22	2.1
1973	1427	29	1.0	2.8	9	0.9	20	1.9
1974	1312	20	1.0	1.7	13	1.2	7	0.5
1975	1237	(9)	0.9	0.8				
1976			0.9	1.4				
1977	1306	12	0.9	1.1				

---

[1] Total CM = Major congenital malformations plus minor congenital malformations
[2] Rate per 100 live births
[3] Major CM
[4] Minor CM

TABLE 7

SUMMARY DATA OF SOFT TISSUE SARCOMA CASES FROM THREE OCCUPATIONAL COHORTS EXPOSED TO 2,3,7,8-TCDD

Year of Birth	1920	1921	1923	1921
Year of Hire	1946	1950	1946	1951
First Exposure	1948	1964	1950	1951
Year of Death	1978	1975	1972	Still alive
Company	Monsanto	Dow	Monsanto	Dow
Process	TCP	TCP	2,4,5-T TCP	TCP
Chloracne	+	±	+	+
Cigarettes	+	+	+	+

TABLE 8

RISK ESTIMATES BY AGENT BY COLLECTION METHOD IN ERIKSSON CASE-CONTROL STUDY

Agent	Questionnaire Alone	Telephone Supplement
Phenoxy Acids and Chlorophenols	---	5.1
Phenoxy Acids Only	---	6.8
Chlorophenols Only	---	3.3
Phenoxy Acids Minus 2,4,5-T and Chlorophenols	---	4.2
Asbestos	1.3	---
Glass Fiber	2.1	---
Power Saws	1.5	---
Smoking	1.1	---
Other Pesticides	2.3	---
Amitrol	2.0	---
Bromofos	2.0	---
DDT	1.3	---
Dinoseb	3.0	---
Fenitrothion	2.0	---
Mercury Seed Rx	1.9	---
Lindane	2.0	---
Na Chlorate	1.0	---
Nicotine	6.1	---
Others	2.1	---

Adapted from: Eriksson M, Berg NO, Hardell L, Moller T and Axelsson O., 1979. Case-Control Study on Malignant Mesenchymal Tumors of the Soft Parts and Exposure to Chemical Substances. Lakartidninger 76:3872-75. (Translated for EPA by Literature Research Company, Annandal , Virginia).

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TOXICITY OF 2,3,7,8-TETRACHLORODIBENZO-P-DIOXIN (TCDD)

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IX. SUMMARY

I. INTRODUCTION

The term "chlorinated dibenzo-p-dioxins" (or more simply, "dioxins") refers to 75 isomers that differ in the number and position of attached chlorine atoms. Each of the 75 chlorinated dioxins that has been studied has its own unique identity and toxicologic properties. 2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD) is considered to be the most toxic of the chlorinated dioxin isomers that have been studied, and it has been comprehensively examined for its toxicological effects. There are 22 possible isomers of tetrachlorodibenzo-p-dioxin. However, the term "TCDD" has been commonly used to mean the 2,3,7,8-tetrachlorodibenzo-p-dioxin isomer without recognizing the existence of the other 21 tetrachloro isomers.

TCDD may be formed in small quantities under certain conditions during the production of 2,4,5-trichlorophenol, and TCDD may be one of the causes of chloracne that has been associated with industrial overexposure during the production of 2,4,5-trichlorophenol. More recently, it has been indicated that various polychlorinated dioxins and furans may be formed during various combustion processes, such as in municipal incinerators, fossil-fueled power plants, internal combustion engines, home fireplaces and cigarette smoke [1, 2]. The present-day knowledge of the magnitude of this issue is somewhat limited.

During this symposium entitled "TCDD Toxicology With Particular Reference to the Seveso Incident," my objective is to review the toxicity of TCDD. In recognition of the very extensive toxicity data base available on TCDD, and the inherent time limitations existent in a symposium, I attempt to review the most pertinent toxicity information in a manner that complements the presentations by the other speakers. As certain aspects of the toxicity of TCDD, especially of the acute and short-term toxicity, have been the subject of several reviews [3-5], my review emphasizes the more recent data available on chronic toxicity, teratogenesis, mutagenesis, reproductive effects, and carcinogenesis. The pharmacokinetics and metabolism will be reviewed in a separate paper at this symposium.

In general, the toxicologic pattern observed with TCDD is not unique; it also occurs with certain halogenated dibenzofurans, chlorinated biphenyls, naphthalenes and brominated dioxins [6].

II. ACUTE AND SUBCHRONIC TOXICITY OF TCDD

The acute toxicity data on TCDD are summarized in Table 1. There are marked interspecies differences in the dose required to produce lethality [3-13]. For example, the single oral dose LD_{50} in the guinea pig is 0.6-2.0 μg/kg [3, 7]. However, in the hamster, TCDD is much less toxic, with an oral LD_{50} of 1157-5051 μg/kg [8, 9]. After administration of a lethal dose, there may be a progressive weight loss and an extended time lapse before death. In monkeys, an early sign of toxicity is swelling of the eyelids, followed by loss of eyelashes, facial alopecia and acnelike eruptions [4, 5, 12]. At necropsy examination, the most constant observations noted in various species are thymic atrophy and general loss of body condition. In acute and subchronic studies, hepatic toxicity is a prominent component of TCDD toxicity in rats, mice and rabbits, but not in monkeys, where effects on the bone marrow and epithelial tissue are more prominent.

Ascites or edema have been noted in mice [11] and chickens [13] given toxic doses of TCDD or certain other compounds. The chick edema bioassay has been based on the ability to elicit marked edema and hydropericardium after exposure of young chicks to these compounds. Subchronic studies have also demonstrated increased excretion of porphyrins in mice [14] and rats [15] treated with higher dose levels of TCDD. Hematologic and clinical chemical findings in acute studies generally reflect the debilitation associated with the acute toxicity of TCDD. In subchronic studies with toxic doses of TCDD in rats, clinical chemistry changes generally reflect the underlying liver toxicity, with increases in serum bilirubin and certain other serum chemistry parameters [15].

In the subchronic toxicity study in rats we conducted in our laboratory, doses of 1.0, 0.1, 0.01 or 0.001 μg TCDD/kg were given 5 days/wk for 13 wk. The highest dose level of 1.0 μg/kg/day caused some mortality, decreased body weights and food consumption, icterus, increased serum bilirubin and alkaline phosphatase, hepatic lesions, thymic atrophy, increased urinary excretion of both porphyrins and δ-amino-levulinic acid, and minimal alterations of some hematopoietic components. The intermediate dose level of 0.1 μg/kg/day had a dose-related decrease in the toxic response. The no-adverse-effect levels were 0.01 and 0.001/μg/kg/day in the 13-week toxicity study [15].

III. STUDIES OF ENZYME INDUCTION AND MECHANISMS OF ACTION

A. Enzyme Induction

Considerable research effort has documented the ability of TCDD to induce hepatic microsomal mixed-function oxidase enzymes of the P-448 variety [16-20]. There appears to be a considerable difference in response from species-to-species, with a rather potent induction of enzymes in rat and mouse, but little or no induction in guinea pig and rabbit [19]. Poland and Kende [21] have drawn attention to the parallelism between the toxic potency of various dioxin isomers and their ability to induce certain enzymes in mice. While this parallelism may exist within certain species, when attempting to generalize between species, there are inherent contradictory factors, especially with the guinea pig, which has the greatest sensitivity to acute TCDD toxicity but which shows little or no induction of enzymes [19]. The extensive research that has been conducted indicates that the induction phenomen is dose related, with the lowest effective single dose of 0.002 μg/kg in the rat [20].

B. Studies on the Mechanism of Action

The high toxicity of TCDD has led to the conduct of numerous studies exploring possible mechanisms of its toxic action. Comparative studies of dioxin isomers indicate the greater toxic potential of certain dioxin isomers involves two properties: (1) halogen atoms occupying at least three of the four lateral ring positions (2, 3, 7, 8 positions) and (2) at least one of the adjacent ring positions being nonhalogenated.

Poland and Glover [22] have identified a cystolic binding protein that they hypothesize acts as the receptor for TCDD to initiate enzyme induction and possibly also toxicity in mice.

A number of parameters have been evaluated as possible mechanisms of TCDD toxicity, Neal et al. [23] have reviewed the results of these studies. At this point in time, the following are considered unlikely explanations of TCDD toxicity: (1) DNA synthesis, after partial hepatectomy [24];

(2) oxidative phosphorylation by liver mitochondria [17]; (3) protein and lipid synthesis [25]; (4) growth capabilities of mammalian cells in culture [26]; (5) thyroid function [23]; (6) intracellular energy production [23]; (7) adrenal glucocortical function and metabolism [23]; and (8) fatty composition of liver, plasma and adipose tissue or metabolism of glucose, alanine, or oleate [23]. Decreased immunocompetence has also been ruled out as the mechanism to explain TCDD Toxicity [13].

A recent study by Poiger & Schlatter [27] indicates that the biologic uptake and toxicity of TCDD is significantly decreased if it is adsorbed onto carbon or soil particles. This new information is very pertinent when assessing possible hazard associated with potential exposure to TCDD.

IV. HISTORICAL REVIEW OF CHLORACNE RESPONSE ASSOCIATED WITH TCDD

A review of TCDD toxicity in humans should begin with historical reports of occupational chloracne dating back to the early 1900s when this skin reaction was incorrectly assumed to be caused by chlorine gas. Chloracne is considered the most consistent response and hallmark of TCDD toxicity in humans. It is now recognized that chloracne can be caused by numerous materials, including polychlorinated dibenzodioxins, polychlorinated dibenzofurans, polychlorinated naphthalenes, polychlorinated biphenyls, tetrachloroazobenzene and tetrachloroazooxybenzene [28]. However, of all these potential acnegenic agents, the best documented is TCDD overexposure associated with industrial production accidents.

In the late 1950s, researchers in Germany established that TCDD was capable of eliciting a chloracnegenic response in humans as well as a positive rabbit ear bioassay. An early review of this work was published by Bauer et al. [29]. Since then there have been additional reports of chloracne associated with industrial production accidents, including the Seveso incident that is the subject of this symposium.

Historically, the use of the rabbit ear bioassay [30] predated analytical capabilities for the detection of compounds with chloracnegenic potential.

The rabbit ear bioassay is based on the ability of acnegenic agents to elicit hyperkeratosis and comedone formation on the inner surface of the rabbit ear. With TCDD, a minimal dose of 0.1-1.0 μg has been reported to induce the acnegenic response [3, 27]. It has been postulated by Greig [31] that the skin areas effected by TCDD of man, rabbit and monkey (and hairless mice) all lack major hair growth, suggesting the possibility that the longer hair shafts on other portions of the body act as an effective wick to assist drainage of sebum and keratinaceous debris from the affected hair follicles.

V. STUDIES OF IMMUNOTOXICITY OF TCDD

The potential of TCDD to alter the immune response was suggested by the observation of thymic atrophy in early toxicity studies with TCDD. Subsequent immunotoxicity studies, which have included both functional and morphologic assessment of humoral and cell-mediated immunity, indicate humoral immunity is less affected by TCDD than cell-mediated immunity. This potential effect appears to be age related, with TCDD exposure during early developmental stages of the immune system being more effective [32]. This effect is also dose related, with the no-adverse-effect level above or near that for other toxic effects.

The mechanism of this effect on cell-mediated immunity has been explored in a number of studies. The thymic atrophy induced by toxic doses of TCDD is not prevented by pretreatment with thymosin [33]. It is not associated with altered zinc levels [33] and is not the result of a direct cytotoxic effect on lymphocytes. Animal studies also indicate this immune toxicity is not mediated by an effect on the pituitary or adrenal gland [34], and that it is not associated with an alteration in growth hormone or food intake [35]. Preliminary surveillance of the human population with documented overexposure to TCDD at Seveso gives little or no indication of resultant immunotoxic effects [36, 37].

VI. TERATOLOGY AND REPRODUCTION STUDIES WITH TCDD

Of the various toxic responses of animals to TCDD, the potential for teratogenicity has perhaps received the most attention. Teratogenic effects resulting from TCDD are rather specific for mice, in which is seen an increased frequency of cleft palate, along with an abnormality (dilatation) of the central collection system of the kidney. The key teratology studies in mice are listed in Table 2 [38-41]. The no-adverse-effect level for teratogenic response in the mouse is 0.1 μg/kg/day [41]. The rat has also been used in teratology studies with TCDD, and these are listed in Table 3 [38, 42, 43]. In the rat, TCDD does not cause a teratogenic effect but does cause embryo- and fetotoxicity. As noted in Table 3, the no-adverse-effect level for rat embryo and fetotoxicity is in the range of 0.03-0.5 μg/kg/day.

Available data on reproduction-type studies of TCDD in monkeys are summarized in Table 4. Initial studies by Allen et al. at the University of Wisconsin [44, 45] reported substantial toxicity, including alopecia, anemia, and death in eight monkeys fed diets containing 500 ppt TCDD for up to 9.3 months. Breeding of the eight female monkeys showing frank toxicity after 6 months of TCDD treatment resulted in two pregnancies, one of which aborted. A preliminary abstract of a follow-up study reported that monkeys given diets containing 50 ppt of TCDD had some slight toxicity, with four of seven pregnancies terminating in abortion [46].

At the present time there are subsequent studies underway at the University of Wisconsin in which monkeys are given diets containing 25 or 5 ppt of TCDD for an extended time period of several years. No information is presently available on these studies in progress. McNulty [47] has reported on studies wherein pregnant monkeys were given TCDD 3 times weekly for 3 wk during gestation. At a high dose level of 0.24 μg/kg/day (∿5000 ppt in diet) abortions occurred in two of two monkeys that had severe toxicity resulting in death. At an intermediate dose level of 0.048 μg/kg/day (∿1000 ppt in diet), abortions occurred in three of four monkeys, with slight maternal toxicity. At a dose level of approximately 0.0095 μg/kg/day (∿200 ppt in diet), no material toxicity was reported, and the abortion rate of 1/4 was comparable to the abortion rate of 3/11 for the control group of monkeys.

Murray et al. [48] reported the results of a 3-generation reproduction study of rats maintained on diets continuously supplying 0.1, 0.01 or 0.001 μg TCDD/kg/day. No significant toxicity was noted in the f_0 male or female rats during the 90 days of TCDD treatment prior to mating. The high dose level of 0.1 μg/kg/day caused decreased fertility and neonatal survival; an intermediate dose level of 0.01 μg/kg/day caused decreased fertility and other effects in the f_1 and f_2 but not f_0 generations. At the dose level of 0.001 μg/kg/day, there was no impairment of reproductive capacity through the three consecutive generations, indicating this to be the no-adverse-effect level.

VII. MUTAGENIC STUDIES WITH TCDD

A. In Vitro Tests in Plant and Microbial Systems

The results of mutagenic studies with TCDD are listed in Tables 5 and 6 [49-52].

Hussain et al. [51] evaluated TCDD for mutagenicity in several bacterial test systems. In tests with Salmonella typhimurium strain TA1530 (for base pair substitution) there was no mutagenic response, but with strain TA1532 (for frameshift mutation) there was an increase in mutational rate, similar to acridine orange. Hussain et al. also [51] reported induction of prophage in Escherichia coli K-39 treated with TCDD. TCDD also appeared to cause some reversion to streptomycin independence in Escherichia coli strain Sd-4, but the data were not well reproduced nor was there a dose-related response.

Seiler [52] tested TCDD in Salmonella strains G46 and TA1530 (both tests for base pair substitution) and TA1531, TA1532 and TA1534 (all tests for frameshifts). He reported TCDD was mutagenic in strain TA1532, of doubtful mutagenicity for strains TA1531 and TA1534, and nonmutagenic in strains G46 and TA1530.

Unpublished work by McCann [49], cited by Wassom et al. [53], reportedly found TCDD to be nonmutagenic both with and without metabolic activation in Salmonella strains TA1532, TA1535, TA1537, and TA1538.

Nebert et al. [50] have also reported negative responses with Salmonella strains TA1535 and TA1538 after treatment with TCDD.

Using a cytologic plant test system (African blood lily) Jackson [54] reported inhibition of mitosis and chromosomal abnormalities after treatment with TCDD. Kondorosi et al. [55] studied the possibility that TCDD might be nucleotoxic by inhibiting transfectivity of bacteriophage. These results showed that TCDD did not inhibit transfectivity similar to other genotoxic agents such as methyl- and ethyl-methane sulfonate, indicating that TCDD did not react (alkylate) viral RNA. Poland and Glover [56] showed very little binding to TCDD rat liver DNA, somewhere in the range of 4-6 orders of magnitude lower than DNA binding observed for most chemical carcinogens.

B. In Vivo Tests in Higher Animals and Man

A number of mutagenic studies in mammals have also been conducted, and the preponderance of data indicates little likelihood of mammalian mutagenesis with TCDD. Green & Moreland [57] reported no evidence of chromosomal aberrations in rat bone marrow after oral intubation of 10 μg/kg of TCDD for 5 consecutive days. In a subsequent study, the TCDD was given orally or intraperitoneally to rats which were killed after 1 or 29 days, again with no evidence of chromosomal changes. The authors concluded that TCDD had no potential for producing chromosomal aberrations in the bone marrow of male rats. Green et al. [58], in a subsequent study with TCDD cited by Wassom et al. [53], reported a statistical increase in the number of chromosomal breaks in the bone marrow of rats given a higher dose when a different experimental protocol was used which did not include control animals. The authors reportedly cautioned that the observed statistical increase should be regarded as only weakly positive for bone marrow chromosomal effects in rats.

Khera & Ruddick [43] reported no dominant lethal mutations in rats afte toxic doses of TCDD were given orally to the males for 7 consecutive days followed by 7 sequential mating trials (each of 5 days' duration).

Beatty et al. [26] reported that TCDD caused no significant effects on mammalian cells in culture. Normal human lymphocytes, normal mouse fibroblasts, normal human fibroblasts, HeLa human epithelial carcinoma cells, SV101 cells, and a derivative of mouse 3T3 cells all showed no changes in morphology or growth pattern after treatment with TCDD.

Results of cytogenetic evaluation of maternal peripheral blood cells and fetal tissues from humans exposed to TCDD at Seveso indicate no mutagenic effects related to TCDD [37, 59, 60].

Thus, while a few positive or questionable mutagenic responses have been observed in certain in vitro plant or microbial test systems, there appear to be no definitive in vivo correlates of mutagenicity in higher animals or man.

VIII. CARCINOGENIC STUDIES OF TCDD

Carcinogenic studies via ingestion of TCDD have been performed in the Sprague-Dawley rat by Kociba et al. [61] and the Osborne-Mendel rat by the

National Cancer Institute [62]. The mouse has been used in studies by the National Cancer Institute [62] and Toth et al. [63]. The results are summarized in Tables 7 and 8.

Review of these data indicates very good correlation of the results in rats and mice, with an oncogenic response associated only with lifetime ingestion of higher dose levels that induce toxicity. The liver was the primary target tissue for oncogenesis in both the rat and mouse. No oncogenic response occurred at dose levels of 0.001-0.0014 μg/kg/day in the rats and 0.001-0.03 μg/kg/day in mice.

In addition to the ingestion studies of oncogenesis, numerous studies of tumor initiation, promotion and cocarcinogenesis have been conducted. These are summarized in Table 9. Mouse skin painting studies by DiGiovanni et al. [64] indicate TCDD to be at most a weak initiator when followed by T-phorbol acetate (TPA) as a promotor, and a rather inactive cocarcinogen when applied with dimethylbenzanthracene (DMBA) followed by TPA. TCDD acted as an inhibitor of tumor initiation when applied in conjunction with either DMBA or benzo(a)pyrene (BAP) in the studies of Cohen et al. [65]. TCDD was not an active promotor of DMBA-initiated mouse skin tumors in studies by Berry et al.[66] and NCI [67].

Pitot et al. [68] conducted a study wherein "the strain of rat and dosage regimen" used were "chosen to resemble closely" the conditions of the 2-yr feeding study by Kociba et al. previously reported [61] as carcinogenic and toxic to the rat liver. The TCDD was given orally to rats after partial hepatectomy and initiation of liver tumors by diethynitrosamine (DEN). Using this test system, Pitot et al. concluded that TCDD was a "potent" promotor of liver tumors in the rat. Pitot et al. also cited the work of Poland & Glover [56] which demonstrated little potential for covalent binding of TCDD to DNA to support their conclusion that TCDD was acting as a promotor rather than an initiator of the hepatocarcinogenesis in rats.

In view of (1) the little likelihood of TCDD to bind covalently to DNA or induce mutagenesis, (2) the well-documented induction of microsomal enzymes, (3) the immunosuppression potential at toxic dose levels, (4) the carcinogenic response occurring in rats and mice at or above dosage levels producing organ toxicity, and (5) the demonstration of Pitot et al. of promotion of DEN-induced tumors in the primary target tissue (liver) of rats, it appears that the predominant mechanism for TCDD carcinogenicity is most likely nongenetic in nature.

IX. SUMMARY

In summary, the toxicity of TCDD has been comprehensively examined in multiple acute, subchronic and chronic studies. Acute toxicity studies have shown marked species differences, with up to a 10,000-fold difference between the single oral LD_{50} dose for the guinea pig and hamster. TCDD is capable of causing an acnegenic response in man and a similar skin response in certain animals. It is also a potent inducer of microsomal enzymes in some but not all species. A dose-related suppression of cell-mediated immunity has been observed at higher dose levels in laboratory animals but not in humans manifesting TCDD-induced acnegenic response.

TCDD causes a dose-related teratogenic response in mice, with the no-adverse-effect level of 0.1 μg TCDD/kg/day.

In rats, TCDD causes embryo- and fetotoxicity above the no-adverse-effect level of 0.03-0.125 μg/kg/day. Dose-related reproductive effects have also been noted in monkeys at doses that elicit maternal toxicity, and additional long-term studies are presently underway. A multigeneration reproduction study as well as a lifetime chronic toxicity study have been completed with TCDD in rats; in both studies, the no-adverse-effect level was found to be 0.001 μg TCDD/kg/day. Numerous mutagenic studies have been performed using in vitro plant and microbial test systems as well as in vivo tests in mammals and man. A mutagenic response was noted in a few of the in vitro test systems, but there are no definitive in vivo correlates of TCDD mutagenicity in higher mammals or man.

TCDD has been studied for carcinogenic potential in rats and mice. There is good correlation of the results, with a carcinogenic response noted in both species only after long-term ingestion of higher dose levels that induce toxicity. No carcinogenic response occurred at continuous dose levels of 0.001-0.0014 μg/kg/day in rats and 0.001-0.03 μg/kg/day in mice.

Data presently available are more supportive of a nongenetic (?promotor) rather than a genetic mechanism of carcinogenesis.

The most recent research, some of which is still underway, indicates that the biologic uptake and toxicity of TCDD may be significantly decreased if the TCDD is adsorbed onto carbon or soil particles. This information is helpful in hazard assessment of exposure to TCDD.

TABLE 1

Acute Toxicity of TCDD

	Single Dose LD_{50} (μg/kg)	Reference
Guinea Pig	0.6-2.0	[3, 7]
Rabbit	115	[3]
Monkey	∿ 70	[4, 5, 12]
Chicken	25-50	[13]
Rat	22-45	[3]
Dog	∿ 100-200	[3]
Mouse	114-284	[7, 11]
Bullfrog	over 1000	[10]
Hamster	1157-5051	[8, 9]

TABLE 2

Summary of Teratology Studies of TCDD in Mice

Strain	Embryotoxic Effects	TCDD Dose Level[a] (μg/kg/day)	Reference
CD-1	Cleft Palate Kidney Abnormality	1,3	[38]
DBA/2J	Cleft Palate Kidney Abnormality	3	[38]
C57BL/6J	Cleft Palate Kidney Abnormality	3	[38]
NMRI	Cleft Palate	3	[39]
C57BL/6	Cleft Palate Dilated Renal Pelvis	1,3	[40]
CF-1	Cleft Palate	$\boxed{0.001, 0.01, 0.1,}$ 1.0, 3.0	[41]

[a] $\boxed{}$ = No-effect levels.

TABLE 3

Summary of Teratology Studies of TCDD in Rats

Strain	Embryotoxic Effects	TCDD Dose Level[a] (μg/kg/day)	Reference
Sprague-Dawley	Intestinal Hemorrhage	$\boxed{0.03,}$ 0.125, 0.5, 2, 8	[42]
CD	Kidney Abnormality	0.5	[38]
Wistar	Hemorrhage	$\boxed{0.125,}$ 0.25, 0.5, 1,2,4,8,16	[43]

[a] $\boxed{}$ = No-effect levels.

TABLE 4

Summary of Reproduction Studies of TCDD in Monkeys

Duration of Treatment	Estimated TCDD Dose Levels		No. Aborted / No. Pregnant	Maternal Effects	Reference
	(ppt in Diet)	(μg/kg/day)			
Up to 9.3 mo	500	0.011	1/2	Generalized Toxicity - Anemia, Hair Loss, Death	[44, 45]
7-20 mo minimum	50	0.0017	4/7	Slight Loss of Weight and Hair in 2/8	[46]
Multiyear	25	Studies Still in Progress			[46]
3 Times Weekly for 3 Weeks of Early Gestation	5000	0.24	2/2	Severe Toxicity & Death	[47]
	1000	0.048	3/4	Slight Toxicity	[47]
	200	0.0095	1/4	No Toxicity	[47]
	0	0	3/11	Control Group	[47]

TABLE 5

Mutagenic Studies With TCDD in Salmonella Bacterial Tests[a]

Strains Assessing Base Pair Substitutions			Strains Assessing Frameshifts					
G46	TA1530	TA1535	TA1531	TA1532	TA1534	TA1537	TA1538	Reference
		-		-		-	-	[49]
		-					-	[50]
	-			+				[51]
	-		?	+	?			[52]

[a] Key: -, negative response; +, positive response; ?, questionable response.

TABLE 6

Mutagenic Studies With TCDD in Test Systems Other Than Salmonella Bacteria[a]

Test	Result	Reference
Prophage induction in E. Coli K-39	+	[51]
Streptomycin Independence in E. Coli Sd-4	+	[51]
Chromosomal Analysis of African Blood Lily	+	[54]
Dominant Lethal Study in Rats	-	[43]
Cytogenetics, Rat Bone Marrow	-	[57]
Cytogenetics, Rat Bone Marrow	?	[58]
Morphology of Human & Animal Cells in Culture	-	[26]
Cytogenetics, Human Blood Cells, Seveso, Italy	-	[37,59,60]

[a] Key: -, negative result; +, positive result; ?, questionable result.

TABLE 7

Carcinogenic Assessment of TCDD in Rats

Calculated Daily Dose TCDD (μg/kg/day)	Rat Strain[a]	Response	Reference
0.1	S-D	Hepatocellular Carcinoma Squamous Carcinoma of Oropharynx and Lung	[61]
0.07	O-M	Hepatocellular Carcinoma Thyroid Tumors	[62]
0.01	S-D	Hepatocellular Nodules	[61]
0.007	O-M	Questionable Increase in Thyroid Tumors	[62]
0.0014	O-M	No Increase in Tumors	[62]
0.001	S-D	No Increase in Tumors	[61]

[a] S-D = Sprague-Dawley; O-M = Osborne-Mendel.

TABLE 8

Carcinogenic Assessment of TCDD in Mice

Calculated Daily Dose TCDD (μg/kg/day)	Mouse Strain (sex)	Response	Reference
1.0	Swiss (M)	No Increase in Tumors, But Decreased Lifespan	[63]
0.3	B6C3F1 (F)	Hepatocellular Tumors/Thyroid Tumors	[62]
0.1	Swiss (M)	Hepatocellular Tumors	[63]
0.07	B6C3F1 (M)	Hepatocellular Tumors	[62]
0.03	B6C3F1 (F)	No Increase in Tumors	[62]
0.007	B6C3F1 (M)	No Increase in Tumors	[62]
0.006	B6C3F1 (F)	No Increase in Tumors	[62]
0.0014	B6C3F1 (M)	No Increase in Tumors	[62]
0.001	Swiss (M)	No Increase in Tumors	[63]

TABLE 9

Studies With TCDD of Tumor Initiation, Promotion, Cocarcinogenesis

Test System	Results	Reference
TCDD on Mouse Skin with TPA as Promotor	TCDD a Weak Initiator	[64]
TCDD+DMBA on Mouse Skin with TPA as Promotor	TCDD a Rather Inactive Cocarcinogen	[64]
TCDD+BAP on Mouse Skin with TPA as Promotor	TCDD Inhibited BAP Tumor Initiation	[65]
TCDD+DMBA on Mouse Skin with TPA as Promotor	TCDD Inhibited DMBA Tumor Initiation	[65]
DMBA on Mouse Skin with TCDD as Promotor	TCDD Not a Promotor of Skin Tumors	[66]
DMBA on Mouse Skin with TCDD as Promotor	TCDD Not a Promotor of Skin Tumors	[67]
TCDD Orally After DEN+Partial Hepatectomy of Rats	TCDD a Promotor of Liver Tumors	[68]
TCDD Given SQ or IP Prior or with MCA Given SQ to Mice	Mixed Response; No Clear-cut Results	[69]

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Dr. BUMB. My name is Robert Bumb. My current job is general manager for Dow Chemical Nederland. I was asked to return from Holland to talk to the members of this subcommittee about chlorinated dioxins and their presence in the environment.

Between 1978 and 1980, I was director of research for the Michigan Division of Dow Chemical USA. In that job, I was responsible for the research and development activities of some 1,000 chemists, engineers, and technicians employed in the scientific research laboratories of the Michigan Division in Midland, Mich.

One of the laboratories in the Michigan Division Research and Development is the analytical laboratory. This laboratory employs some 240 highly skilled analytical scientists. Among the many analytical techniques that were developed by this group were the innovative analytical techniques for the qualitative detection and quantitative measurement of chlorinated dioxins, particularly the 2,3,7,8-TCDD isomer, in environmental samples.

My testimony today to the subcommittee describes the results of the use of these innovative analytical techniques for the detection and measurement of chlorinated dioxins in the environment. The results of these analyses were originally published in a paper by Dow entitled, "Trace Chemistries of Fire: A Source of Chlorinated Dioxins." This report, which was released in 1978, was published in Science in 1980.

The report details the presence of chlorinated dioxins in the environment. Specific analysis of soil samples, exhaust mufflers of diesel engines, soot in fireplaces, charcoal broiled steaks, cigarettes, refuse incinerators, fossil fuel powerhouse soot, and home electrostatic precipitators document the presence of chlorinated dioxins in the U.S. environment. When we released the report, we hypothesized that chlorinated dioxins were trace products of combustion processes. As you, the subcommittee, probably know, at that time the report, our hypothesis, and our scientists were subjected to vocal and harsh criticism.

Since that time, there have been over 58 separate publications which continue to document the presence of chlorinated dioxins in the environment and the world and to support our original hypothesis that combustion processes produce the trace amounts of chlorinated dioxins.

Chlorinated dioxins have been found in fireplaces from homes in New Hampshire, Oregon, Minnesota, and Michigan. The dioxins have been found in gulls' eggs in remote parts in Canada and in fat of Canadian seals. They have been found in Japan, Holland, Switzerland, Tennessee, and Chicago. Our original claim that chlorinated dioxins are ubiquitous in the environment and that they are trace products of combustion is strongly supported and continues to gain support.

Mr. Chairman, members of the subcommittee, thank you for allowing me to speak.

[The prepared statement of Dr. Bumb follows:]

TESTIMONY ON THE ANALYTICAL CHEMISTRY OF DIOXIN BY DR. ROBERT R. BUMB

SUMMARY

In November 1978, Dow announced the discovery that chlorinated dioxins are ubiquitous in the environment. It was concluded that the presence of dioxin is due to the existence of a natural phenomenon, called trace chemistries of fire.

Trace chemistries of fire consists of numerous chemical reactions occurring during normal combustion at very low concentrations, parts per million and lower. The measurable yields of the trace chemical reactions can be as low as 0.0000000001 percent.

The Trace Chemistries of Fire follow two pathways--chemicals reacting at very low yields and low concentration chemicals reacting at high yields.

Based on the results of our study, we concluded:

1. Refuse incinerators and fossil-fuel powerhouses can be sources of particulates which contain dioxins;
2. Gasoline and diesel-powered car and truck mufflers are sources of airborne particulates which contain dioxins; and
3. Soot from the burning of wood in fireplaces contain dioxin.

The study titled, "Trace Chemistries of Fire: A Source of Chlorinated Dioxins," was published in Science Magazine in 1980.

Since 1980, there have been three international conferences on the subject. The international scientific community generally accepts the fact that dioxins are produced in common combustion

U.S. Food and Drug Administration
U.S. Environmental Protection Agency
U.S. Department of Agriculture
Center for Disease Control
New York State Department of Public Health
Michigan Department of Agriculture
Michigan Department of Natural Resources
Ontario Ministry of the Environment
Battelle
Hooker Chemical
C. H. Boehringer Sohn, Germany
University of Utah
University of Nebraska
Wright State University
Michigan State University
University of New Orleans
University of Umea, Sweden
University of Amsterdam, The Netherlands

processes. Fifty-eight papers have been published on the subject. Dioxins have been found in emissions from municipal incinerators around the United States, in Canada, the Netherlands, Italy, and Switzerland, Sweden and Japan.

In 1982, Dow conducted a study of soot from woodburning stoves which was published in Analytical Chemistry. Several stoves were sampled in each of three different locations including New Hampshire, Minnesota, Oregon and Michigan. Dioxins were present to varying degrees in the soot from all stoves sampled. The findings suggest that dioxins are entering the environment via the burning of wood from coast-to-coast across the U.S.

In fact, dioxins have probably been in the environment since the advent of fire. Only during the past several years has the sophisticated, sensitive analytical methodology developed the abilities to detect the minute concentrations.

Dow developed this methodology and has improved its analytical expertise in dioxin research. Dow has freely and openly assisted many other researchers in industry, academia, and government agencies develop their own capabilities. Dow has worked closely with a number of organizations, sharing our analytical technology with all who have asked for it. These include:

THE DIOXINS

There are 75 chlorinated dibenzo-p-dioxins or CDDs. These have commonly been referred to as "dioxins". This family of dioxins is structurally similar, but the molecular formulas and chemical properties of the compounds vary. Each member of the dioxin family consists of an aromatic molecule of two benzene rings bonded together as shown in Figure 1. Varying combinations of hydrogen and chlorine atoms in the eight free external positions (number 1,2,3,4,6,7,8,9)[1] can be attached to the ring, thus creating different categories of dioxin.

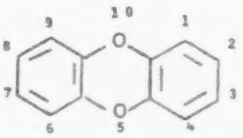

Figure 1

Molecular structure of dibenzo-p-dioxin

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[1] In the dibenzo-p-dioxins, the 5 and 10 positions are occupied by oxygen atoms to which the benzene ring structures are attached.

Compounds containing the same number of atoms--in this case, chlorine atoms--attached at different positions are called "isomers." Each isomer, while having the same molecular formula has unique and varying chemical properties.

The tetrachlorodibenzo-p-dioxins (TCDDs) consist of the largest number of isomers as a group--twenty-two. Included within this group is the 2,3,7,8-tetrachlorodibenzo-p-dioxin (2,3,7,8-TCDD) isomer.

While residues of this 2,3,7,8-TCDD isomer have been reported in environmental samples during the past several years, analytical chemists have only recently been able to isolate and identify all of the other 21 TCDD isomers and thus have only recently had the capability to determine the unique presence of the 2,3,7,8-isomer. (Ref. 1) In 1979, our analytical laboratory was the first to develop this capability, and today remains one of the few laboratories with the ability to identify each of the 22 TCDD isomers in environmental samples. The preparation of even minute quantities of these other TCDDs for use as standards in the analysis of environmental samples involves time-consuming and expensive procedures. Dow has done significant research on this topic. One of the most extensive studies was completed in 1978.

THE TRACE CHEMISTRIES OF FIRE REPORT

A. BACKGROUND

In 1978, the Environmental Services Group of the Michigan Division was preparing a report dealing with the results of analyses on fish from the Tittabawassee River, a river which flows past Dow's Michigan Division plants. The analyses indicated that fish contained trace amounts of one or more isomers of TCDD, as well as other chlorinated compounds such as higher chlorinated dibenzo-p-dioxins, polychlorinated biphenyls, polybrominated biphenols, and others. The report regarding these analyses (Appendix A) was delivered to the Department of Natural Resources of the State of Michigan and to EPA in mid-June of 1978.

At that time, 2,4,5-trichlorophenol and products made from trichlorophenol were generally believed to be the only sources of TCDD. Because Dow's facility manufactured the product and had an outfall to the river, this was suspected of being the origin of the 2,3,7,8-TCDD in these fish through the outfall to the river.

Nevertheless, TCDD had been detected only once during regular sampling of Dow's tertiary effluent and has not been detected since with our current regulatory state-of-the-art analytical methodology. Due to the extreme sensitivity of the method, we contend that only data must be closely scrutinized as to the validity of its findings and methods. Hence, a task force of Dow scientists was formed to investigate the source or sources of this 2,3,7,8-TCDD.

The Dow Chlorinated Dioxin Task Force quickly met with a number of State government employees in Midland on July 11, 1978, to discuss our data on fish, the chemistry and manufacturing processes at Dow involved with trichlorophenol processing, and the plans of the Task Force to find the source or sources of TCDD. This meeting concluded with our commitment to determine the sources of TCDD and to keep the State agencies informed of our progress.

We set out to determine where dioxin occurred in the environment. We had already received information indicating that dioxins may be found in many locations. In mid-1978, Dow chemists had discovered TCDD and other dioxins in dust samples collected from our Analytical Laboratories. Dioxins were found even in those samples collected after careful cleaning. This suggested that airborne particulate matter may be a source of TCDD in the environment. These findings were surprising, because we were looking for a water-borne source.

In addition, a sampling procedure was developed to collect dust and soil samples from rural and urban areas in Michigan and several other states to serve as control samples. As we continued to find various dioxins in all of these samples, we undertook the analysis of additional environmental samples to further determine where TCDD and other chlorinated dioxins exist.

About this same time, we also learned of the research of Professors Christopher Rappe in Sweden and Otto Hutzinger in the Netherlands. (Refs. 2 and 3) Dr. Rappe had reported that the incomplete combustion of chlorophenols led to the formation of TCDD, other dioxins and other compounds. Similarly, Dr. Hutzinger had observed dioxins in municipal incinerator fly ash. (Ref. 3) He hypothesized that the chlorinated dioxins might be formed as a result of combustion and might not require a trichlorophenol precursor. We, therefore, also tested diverse combustion sources for the presence of dioxins to determine the source of chlorinated dioxins in the environment.

The results of our investigation of environmental samples were announced in a Dow report, "The Trace Chemistries of Fire--A Source of and Routes for the Entry of Chlorinated Dioxins into the Environment," in November 1978. This study was immediately forwarded to EPA and the State of Michigan for their review (Appendix A). We reported that we had found TCDD and other chlorinated dioxins in samples from dust, soil, incinerators, powerhouses, wastewater treatment sludge, truck and auto mufflers, fireplace soot, a residential electrostatic precipitator, cigarette smoke and charcoal broiled steaks. Dioxins, including TCDD, were found in areas as diverse as Midland, Chicago, St. Louis, Detroit and Nashville. Our results are summarized in Table I. [Note the amounts shown in Table I are in parts per billion (ppb)].

As shown in Table I, the levels of TCDD found varied from not detected to 120 ppb (120,000 ppt), although most TCDD findings were in the low ppt range. For example, a diesel truck muffler contained 23 ppt of TCDD; auto mufflers, 8 ppt; and home fireplace soot, 400 ppt. A municipal incinerator located in Nashville, Tennessee contained 7.7 ppb (7,700 ppt) TCDD.

During the course of our investigation of particulate samples, we improved our analytical procedures to the point that we were finally able to separately identify all 22 TCDD isomers from one another. (Ref. 1) Using these techniques, we re-analyzed many samples which had shown positive TCDD residues. In most cases we discovered, as we expected, that what was originally reported as TCDD consisted of numerous TCDD isomers. Indeed, often the other isomers represented a greater percentage of the total TCDD observed than the 2,3,7,8-TCDD isomer. For example, while 7,700 ppt total TCDD were found in the electrostatic precipitator from the Nashville, Tennessee municipal incinerator, 2,3,7,8-TCDD plus possibly eleven other isomers comprised only 400 ppt (5.2%) of this sample.

"Trace Chemistries of Fire" predicts that TCDD is stable below 800°C. If the fuel is supplemented by natural gas, for example, to raise and maintain the flame temperature above 1000°C, then the formation of TCDD is minimized and the destruction is maximized. It appears that formation of dioxins cannot be completely eliminated only minimized.

Most industrial incinerators operate with supplemental fuel and, hence, at temperatures above 1000°C. We did not detect 2,3,7,8-TCDD or any tetra isomers in our own rotary kiln incinerator or tar burner operating under these conditions.

EPA's study of five municipal incinerators which operate at lower temperatures support our observation on municipal incinerators (Appendix B). The only data available on commercial incinerators was generated by EPA at two commercial units. In both of these studies, EPA concluded there was nc risk to human health from dioxins found in these emissions (Appendix C).

Based on these results, we concluded the following:

1. Refuse incinerators and fossil-fuel powerhouses can be sources of particulates which contain TCDD and other dioxins;

2. Gasoline and diesel powered car and truck mufflers contain airborne particulates containing TCDD and other dioxins;

3. Some fireplaces also contain particulate matter containing TCDD and other dioxins.

As is noted in the "Trace Chemistries" report, these samples do not represent anything other than the particular samples taken. Because they were not taken by a statistically designed methodology, they cannot be used, nor were they meant to be used, to predict precise quantitative amounts of TCDD in the overall environment.

In reporting these results, we were cautious to indicate that the data were not comprehensive or exhaustive findings. Neither were they statistically significant; they represent a small number of samples, with a large number of variables which could not be controlled adequately. Indeed, our purpose was primarily to suggest multiple sources of dioxins in the environment, and to stimulate further research.

Despite these limitations, we feel these data do show that TCDD and other dioxins are ubiquitous in the environment.

Having given you this background, let me describe the development of events since that time.

DEVELOPMENTS AFTER THE TRACE CHEMISTRIES REPORT

A. REVIEW BY AN EXPERT SCIENTIFIC PANEL

While all Dow reports undergo fairly rigorous internal scientific peer review within the Company, we decided that it would be useful to seek additional, independent peer review of these important results. Consequently, we asked a panel of independent and respected scientists to inspect, review and question our work. That panel was chaired by Dr. Lockhart B. Rogers, Graham Perdue Professor of Chemistry, University of Georgia, and a member of the analytical advisory committees of the National Research

Council, the Oak Ridge National Laboratory and a holder of many other prestigious posts in analytical chemistry.

The Rogers Panel issued its report in June 1979. They concluded that our sampling techniques were suitable, that our analytical technology was "state-of-the-art," and that the results of our analyses were valid qualitatively and quantitatively:

The Panel did not take a formal position on the reason or reasons for the presence of chlorinated dioxins in the environment. Rather, they correctly noted the need for more work to confirm the Dow procedures and results. Appendix D is the Panel's non-technical summary discussion. As seen in this Appendix, the work on the trace chemistries of fire has progressed greatly since our report, with TCDD and other dioxins being found regularly by others.

B. PUBLICATION OF THE REPORT

The report entitled, "Trace Chemistries of Fire: A Source of Chlorinated Dioxins", was published in Science in 1980 after receiving peer review from several eminent scientists (Appendix E).

C. DEBATE CONCERNING PRECURSORS

In the two-year period after the "Trace Chemistries" report was made public, most researchers worldwide concluded that dioxins are formed via combustion. The primary questions regarding the conclusions of "Trace Chemistries" have therefore centered on which compounds must be precursors to the formation of TCDD and other dioxins in combustion processes. For example, some researchers have attributed the presence of the dioxins in municipal incinerators to the combustion of chlorinated phenols and chlorinated diphenyl ethers. Drs. Lustenhouwer, Olie and Hutzinger include as precursors all polychlorinated benzenes, polychlorinated biphenyls (PCBs), phenols and polyvinyl chloride (PVC). This is significant since PVC is a non-aromatic compound which nevertheless yields dioxins upon pyrolysis. (Ref. 4)

D. COAL COMBUSTION

Research at Dow shows that TCDD and other dioxins are formed as a result of the combustion of coal alone and in combination with various natural chlorine donors. As can be seen in Table II, each experiment in which coal was combusted resulted in the formation of chlorinated dioxins. TCDD was formed in large quantities when coal was pyrolized in the presence of hydrochloric acid and chlorine gas. (Ref. 5 and Appendix F) These data indicate that coal in the presence of chlorine donors is also a precursor of TCDD and other dioxins.

E. WOODBURNING COMBUSTION

Other research has confirmed the combustion theory. A paper has been published in Analytical Chemistry describing the isomer-specific determination of TCDD's and higher chlorinated dioxins in chimney soot from wood-fueled domestic stoves. (Ref. 6 and Appendix G) We conducted this study to support our theory that dioxins have been present in the environment since the advent of fire. Several wood-fueled stoves were selected in three different geographical locations across the United States; including near Farmingham, New Hampshire; Duluth and Grand Marais, Minnesota; near Portland, Oregon; and near Garden and Midland, Michigan. The history of each stove and woodlot was carefully investigated.

The data (shown in Table IIIa-IIIe) can be summarized as follows: at least 20 of the 22 tetra isomers were found at levels (total tetra) which varied from not detected to as high as 5,000 ppt. The 2,3,7,8 isomer was found at levels as high as 200 ppt. The hexachloro-dioxin levels varied from 3 ppt up to 4500 ppt. The hepta levels varied from a 9 ppt up to 9000 ppt. The octachlorodioxin levels varied from 14 ppt to 15,400 ppt.

F. HISTORICAL EVIDENCE OF CHLORINATED DIOXINS IN THE ENVIRONMENT PREDATING COMMERCIAL CHLOROPHENOLS PRODUCTION

A sample of Milorganite™ (dried municipal waste treatment sludge from Milwaukee, WI), that was sealed in glass for display at the Chicago World's Fair in 1933, has been graciously provided by the Milwaukee Metropolitan Sewerage District for chemical analysis. This material was representative of typical municipal waste treatment sludge of that period.

An examination of the chemical industry literature indicates that widespread commercial production and use of chlorophenols and their derivatives began in approximately 1935. No chlorinated plastics were in commerce at that time. Phenoxy herbicides were not produced until the 1940's. Therefore, the examination of an environmentally significant sample for chlorinated dioxins content collected prior to 1935 should provide a measure of historical evidence regarding the "so-called" natural presence of chlorinated dioxins.

Analytical examination of this preserved sample from 1933 indicates a broad spectum of chlorinated dioxins present at part per billion concentrations (Table IV). While comparison of the chlorinated dioxins content of the 1933 samples with current production material from 1981 and 1982 does indicate an increase for lower chlorinated congeners in the latter, the total chlorinated dioxins content is nominally equivalent. (Ref. 7 and Appendix H)

G. THE IMPACT OF THE ENVIRONMENT ON AIRBORNE PARTICULATE MATTER FROM THE ERUPTION OF MOUNT ST. HELENS

Although the release of massive amounts of particulate matter into the atmosphere arising from the eruption of Mount St. Helens may be considered environmentally detrimental by many, the circumstances surrounding this geological event were unique from a scientific point of view. The observation, that freshly emitted particulates from a nearly uninhabited source were essentially free of organic contaminants typically found in the surrounding environment, presented an opportunity to investigate atmospheric interactions with transient particulate matter under "real world" conditions. These limited data seem to confirm that clean particles passing through dirty air become contaminated.

Approximately 50 groundfall ash samples were collected during the period of June 1 to June 12, 1980, from which the 12 presented in Table (V) were selected for analysis. Samples were subjectively grouped into four different categories on the basis of their collection-point environmental conditions. The blast zone samples were collected by United States Geological Survey personnel. These samples were characteristic of particulate matter deposited in the area of complete devastation on the northern side of Mount St. Helens within sight of the crater. The unit A material was classified as blast-related fallout, and the unit C sample was exemplary of particulates related to pyroclastic flow that were deposited while hot. Rural zone samples were obtained from locations reasonably distant from permanent habitations and major highways. Samples collected immediately adjacent to interstate thoroughfares bearing heavy motor traffic on a regular basis were defined as interstate highway zones. As shown in Table (VI), none of the samples in this category were taken from areas where expected contamination sources other than the highway traffic were evident. The urban samples were collected from areas within a city where habitations, motor traffic, and industrial activity were prevalent. Also included in Table (V) are the estimated environmental exposure times for each sample. Because two eruptions occurred prior to sample collection, one on May 18 and the other on May 25, it is impossible to accurately define the "age" of these particulates.

The volcanic emissions were free of polychlorinated biphenyls, polynuclear aromatics and chlorinated dioxins upon exiting the source, and remained so throughout their period of deposition in the blast zone. Particle/organic association for these compounds demonstrate an increasing concentration profile for polynuclear aromatic compounds, polychlorinated biphenyls and chlorinated dioxins when the sampling location was moved from rural to urban environments. (Ref. 8 and Appendix I)

H. FISH BIOAVAILABILITY STUDY

Dow had recently contracted with Wright State University for a Fundamental Combustion Study (Appendix J). Wright State also proposed to Dow a second study to determine if dioxins from flyash were bioavailable to fish. Because of our previous commitment with Wright, we asked and obtained their permission to send their protocol to EPA for review and possible funding. Neither Dow nor EPA had funds available to externally support this study. It was agreed that EPA would do the fish exposure and provide the flyash, Dow would provide the analytical expertise, and Wright State and EPA would perform check analysis on Dow. A Wright State graduate student was invited by EPA to participate in the fish studies at Duluth.

A protocol was generated (Appendix K). EPA conducted a preliminary experiment with carp fingerlings and flyash from a municipal incinerator. The flyash was analyzed by Dow before the experiment and the fish were analyzed after being exposed to the flyash for 30 days. The original flyash contained a very small amount of 2,3,7,8-TCDD (.48% of the total tetrachloro isomers), all 21 other tetrachloro isomers, hexa-, hepta-, and octachlorodioxins.

The exposed fish contained mostly 2,3,7,8-TCDD (84%), small amounts of a few other tetra isomers, and hexa-, hepta- and octachlorodioxins. The data are summarized in Table VII.

Based on the preliminary experiment, a controlled experiment was performed with carp fingerlings and a composite of flyash from four different municiple incinerators. Again, Dow analyzed the composite flyash. The dioxin levels in this flyash were significantly higher than the flyash used in the preliminary experiment. Based on these data, EPA decreased the dose level and shortened the exposure time.

Fish exposed to this flyash for up to 30 days showed very low levels of dioxins by the Dow method and not detected levels by EPA. Wright State was not sent check samples because of these results. Samples analyzed by Dow included controls and were blind analyzed (Appendix L).

Later, the composite flyash was analyzed for metals and carbon content. The carbon content was significantly higher in the composite flyash than in flyash used in the preliminary experiment. Past experience by EPA, Dow and others has shown that carbon holds onto dioxins tenaciously.

A definitive experiment should be done to resolve this issue. This experiment is in the planning stage.

I. OTHER CONFIRMATORY DATA

Since our work in 1978, confirmation of the "Trace Chemistries" hypothesis has been proceeding throughout the world. More than 58 papers from several countries have been published on the subject (Appendix M). Over 20 published articles now describe dioxin emissions from municipal incinerators in the U.S.A., Canada, The Netherlands, Italy, and Switzerland.

Since 1980, there have been three International Dioxin Conferences "Trace Chemistries of Fire" is generally accepted . the scientific community. Our findings have been confirmed by many researchers in the U.S., Canada, Europe and Japan.

Several theoretical and laboratory studies have been reported describing the chemistry behind the "Trace Chemistries" hypothesis. For example, Choudhry, (Ref. 9) et al, have described several possible formation mechanisms for dioxins during combustion. Eiceman (Ref. 10) has discovered and demonstrated how dioxins may undergo chlorination during the emission process. This confirms part of Townsend's (Ref. 11) Redox hypothesis, which describes dioxins physical chemistry and occurrence of dioxins in the environment.

CONCLUSION

Dow and other researchers around the world have analyzed thousands of environmental samples and learned that the chlorinated dioxins, including TCDD, are virtually ubiquitous worldwide.

In particular, we discovered dioxins in dust, soil, and chimney soot from many diverse rural and urban locations throughout the United States. In addition, we identified 2,3,7,8-TCDD and/or other dioxins in all samples tested from combustion sources, such as municipal incinerators, powerhouses, truck and auto mufflers, fireplace soot, cigarette smoke, and even charcoal broiled steaks. We reported that information in 1978 and it was subsequently published in 1980. Other Dow studies have been published since then and some are still in progress.

Three International Dioxin Conferences have been held since 1980. Much of our findings have been corroborated by other scientists, and the fact that dioxins are produced by fire is generally accepted by the scientific community.

Dioxins have probably been in the environment since the advent of fire. Analytical methodology sensitive enough to detect these dioxins has been developed only during the past several years.

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APPENDIX M - Literature Search on Publications Dealing with the "Trace Chemistries of Fire"

TABLE I. - Chlorinated Dioxins in the Environment

Sample	Number of samples	Apparent dioxin content, ng/g (ppb)*					
		TCDD			HCDD	H_7CDD	OCDD
		Other isomers	2,3,7,8-	Total			
Soil							
Rural (Gaylord, Michigan)	5			N.D.†	N.D.	N.D.–0.05	N.D.–0.2
Urban (Lansing and East Lansing, Michigan)	5			N.D.	0.03–1.2	0.03–2	0.05–2
Major metropolitan (Chicago, Illinois)	8			0.005–0.03	0.03–0.3	0.1–3	0.4–22
Dow Chemical (Midland, Michigan)	5	0.6–18	0.3–100	1–120	7–280	70–3,200	490–20,000
Dust							
Dow Chemical laboratory	6	0.5–2	0.7–3	1–4	9–35	140–1,200	650–7,500
Midland, Michigan	2			0.03–0.04 (0.02)	0.2–0.4	2–4	20–30
Metropolitan (Detroit, Michigan)	4			N.D.–0.02	N.D.–0.3	0.3–4	0.1–4
Metropolitan (St. Louis, Missouri)	1	0.16	0.12	0.3	2	34	210
Metropolitan (Chicago, Illinois)	2			0.04 (0.04)	N.D.–0.3	0.6–3	3–8
Wastewater treatment sludge							
Commercial sludge fertilizer (Milwaukee, Wisconsin)	1	0.29	0.02	0.31	2	30	180
Incinerators, powerhouse							
Dow powerhouse	1	38 (20)	N.D. (10)	38 (20)	2	4	24
Dow rotary incinerator stack (present normal operation with supplemental fuel)‡	5			N.D. (2)	1–5	4–100	9–950
Dow stationary tar burner stack (normal operation with supplemental fuel)	5	N.D.	N.D.	N.D.	1–20	27–160	190–440
U.S. municipal incinerator (electrostatic precipitator) (Nashville, Tennessee)	1	7.3	0.4	7.7	14	28	30
European municipal incinerators				2–20	30–200	60–130	40–120
Mufflers							
Diesel truck muffler	2	0.02	0.003	0.023	0.020	0.100	0.26
Auto muffler	4	N.D.–0.004	N.D.–0.004	N.D.–0.008	N.D.	0.005–0.01	0.02–0.07
Other sources							
Home fireplace soot	2	N.D.–0.3	N.D.–0.1	N.D.–0.4	0.2–3	0.7–16	0.9–25
Home electrostatic precipitator	1	0.4 (0.4)	0.6	1.0	34	430	1,300
Cigarette smoke	2	N.D.	N.D.	N.D.	0.004–0.008	0.009	0.02–0.05
Charcoal-broiled steak	4	N.D.	N.D.	N.D.	N.D.	N.D.	0.03 (0.03)

*Where multiple samples were analyzed from similar sources, the range of observed values is shown. †N.D. indicates that the signal observed was less than 2.5 times noise. Limits of detection generally observed were TCDD, 0.001 to 0.01 ppb; HCDD, 0.01 to 0.05 ppb; H_7CDD, 0.005 to 0.03 ppb; and OCDD, 0.01 to 0.05 ppb. Limits of detection not within these ranges are shown parenthetically after the value reported for signals between 2.5 and 10 times noise. ‡Data without supplemental fuel not included here because this practice has been eliminated.

TABLE II

Summary of Chlorodibenzo-p-Dioxins Detected after High Temperature Oxidation and Chlorination of Coal

Experiment		Amount of Chlorodioxin Species Present[a]			
Material	High Temperature Reaction	Tetra[b] (ppb)	Hexa (ppb)	Hepta (ppb)	Octa (ppt)
1. Coal	No	ND(0.07)[c]	ND(0.03)	ND(0.1)	ND(0.3)
2. HCl	No	ND(0.003)	ND(0.01)	ND(0.03)	ND(0.03)
3. Cl_2 + Air[d]	Yes				
A. Tube		ND(0.07)	ND(0.2)	ND(0.3)	ND(0.5)
B. Trap		Int.[e]	ND(0.2)	ND(0.3)	ND(0.4)
Sum		ND(0.07)	ND(0.2)	ND(0.3)	ND(0.5)
4. Coal + Air	Yes				
A. Tube		ND(0.08)	ND(0.1)	0.2(0.2)	ND(0.7)
B. Trap		ND(0.06)	ND(0.1)	0.4(0.3)	1.3(0.4)
Sum		ND(0.08)	ND(0.1)	0.6(0.3)	1.3(0.7)
5. Coal + Air + NaCl	Yes				
A. Tube		ND(0.06)	ND(0.09)	0.2(0.2)	1.3(0.3)
B. Trap		ND(0.07)	ND(0.2)	0.3(0.2)	1.4(0.5)
Sum		ND(0.07)	ND(0.2)	0.5(0.2)	2.7(0.5)
6. Coal + Air + HCl	Yes				
A. Tube		0.45(0.06)	5.0(0.1)	21(0.3)	61(0.5)
B. Trap		1.0(0.06)	3.4(0.1)	4.1(0.3)	2.5(0.6)
Sum		1.4(0.06)	8.4(0.1)	25(0.3)	64(0.6)
7. Coal + Air + Cl_2	Yes				
A. Tube		ND(0.3)	7.1(0.2)	20(0.6)	57(1)
B. Trap		1.2(0.3)	22(0.4)	71(2)	230(3)
Sum		1.2(0.3)	29(0.4)	91(2)	290(3)

(a) Data not corrected for recovery.
(b) ppb = ng of chlorodioxin/g of coal-starting material.
(c) ND = not detected; (X.XX) = detection limit.
(d) Results normalized to a 2 gram sample.
(e) Int. = Interference.

TABLE III. A - CDDs in Parts per Trillion for Eastern Region
RWC Unit Chimney Particulates

	eastern						
	no. 1	no. 7	no. 3	no. 5	no. 2	no. 6	reagent blank
chimney type	masonry	masonry	masonry	masonry	masonry	masonry	
sampling point	base	base	base	base	base	base	
primary fuel	red oak	red oak	red oak	red oak	red oak	red oak	
operation[a]	high	low	high	high	high	high	
^{13}C-2378-TCDD recovery	80%	63%	69%	71%	82%	72%	72%
2378-TCDD	ND[d] (0.8)	160	130	106	ND (1.1)	1.3 (0.6)	ND (0.8)
1469-TCDD	ND (1.4)	44	12 (2.9)	9.6	ND (0.8)	ND (0.8)	ND (1.1)
1269-TCDD	ND (1.4)	220	52	73	ND (0.8)	1.0 (0.8)	ND (1.1)
1267-TCDD	ND (1.4)	150	35	62	ND (0.8)	ND (0.8)	ND (1.1)
1289-TCDD	ND (1.4)	170	36	73	ND (0.8)	ND (0.8)	ND (1.1)
1369-TCDD	ND (1.1)	330	57 (11)	77	ND (1.0)	1.5 (0.7)	ND (1.4)
1247 + 1248-TCDDs	ND (1.1)	760	110	230	ND (1.0)	2.9 (0.7)	ND (1.4)
1278-TCDD	ND (1.1)	460	84 (11)	130	ND (1.0)	1.5 (0.7)	ND (1.4)
1268-TCDD	ND (1.1)	510	86 (11)	140	ND (1.0)	2.1 (0.7)	ND (1.4)
1237 + 1238-TCDDs	ND (1.1)	860	120	250	1.2 (1.0)	3.3 (0.7)	ND (1.4)
1279-TCDD	ND (1.1)	380	110	210	ND (1.0)	1.4 (0.7)	ND (1.4)
"1246"-TCDD[b]	ND (0.9)	210	49 (6.4)	130	ND (1.0)	1.1 (1.0)	ND (1.4)
1478-TCDD	ND (0.9)	100	17 (6.4)	83	ND (1.0)	ND (1.0)	ND (1.4)
1236-TCDD	ND (0.9)	250	52 (6.4)	120	ND (1.0)	1.0 (1.0)	ND (1.4)
1239-TCDD	ND (0.9)	240	49 (6.4)	140	ND (1.0)	ND (1.0)	ND (1.4)
"1249"-TCDD[b]	ND (1.0)	240	43 (7.1)	100	ND (0.8)	1.5 (0.8)	ND (1.4)
1368-TCDD	ND (2.1)	840	86 (9.7)	130	2.5 (0.8)	26	ND (1.0)
1379-TCDD	1.6 (1.0)	980	110	120	2.7 (0.8)	19	ND (1.0)
1378-TCDD	ND (1.0)	620	200	210	ND (0.8)	3.2 (0.8)	ND (1.0)
1234-TCDD	ND (1.0)	300	67	120	ND (0.8)	2.0 (0.8)	ND (1.0)
total TCDDs	1.6	7824	1505	2513.6	7.4	68.8	ND
isomers obsd	1	20	20	20	3	15	0
^{13}C-HCDD recovery	76%	76%	77%	89%	87%	56%	67%
124679 + 124689-HCDDs	5.4 (4.1)	740	530	620	5.7 (1.6)	18 (3.4)	ND (4.5)
123468-HCDD	ND (4.1)	1800	210	420	2.4 (1.6)	27 (3.4)	ND (4.5)
123679 + 123689-HCDDs	11 (4.1)	2000	1100	2800	15 (1.6)	48	ND (4.5)
123469-HCDD	ND (4.1)	ND (160)	ND (90)	ND (90)	ND (1.6)	ND (4.1)	ND (4.5)
123478 + 123678-HCDDs	4.7 (4.1)	530	300	650	4.5 (1.6)	11 (3.4)	ND (4.5)
123467 + 123789-HCDDs	ND (4.1)	530	260	440	4.7 (1.6)	12 (3.4)	ND (4.5)
total HCDDs	21.1	5600	2400	4930	32.3	116	ND
H$_7$CDD corr factor[c]	67%	68%	76%	86%	88%	62%	64%
1234679-H$_7$CDD	27	2100	2500	1000	30	110	ND (3.1)
1234678-H$_7$CDD	36	2100	2900	1700	35	84	ND (3.1)
total H$_7$CDDs	63	4200	5400	2700	65	194	ND
^{13}C-OCDD recovery	58%	60%	74%	83%	79%	68%	60%
OCDD	95	3400	7200	1200	110	190	ND (5.0)

[a] Typical mode of RWC unit operation where low designates low air-restriction (hot fire) and high designates high air-restriction (airtight operation). [b] May be either 1246- or 1249-TCDD. [c] Average of internal standard recoveries for ^{13}C-123478-HCDD and ^{13}C-OCDD. [d] Indicates component was not detected at the limit of detection (LOD) in parentheses. If the LOD (defined as 2.5 × peak-to-valley noise) is less than 10% of the observed component, it is not reported.

TABLE III. B - CDDs in Parts per Trillion for Western Region RWC Unit Chimney Particulates

	western						
	no. 10	no. 12	no. 17	no. 18	no. 11	no. 14	reagent blank
chimney type	metal	metal	metal	masonry	metal	metal	
sampling point	top	top	top	top	top	top	
primary fuel	fir	fir	oak	fir	fir	fir	
operation[a]	low	low	high	high	high	high	
^{13}C-2378-TCDD recovery	74%	62%	74%	61%	63%	71%	57%
2378-TCDD	8.0	18	6.4 (1.2)	18	9.2 (1.3)	20	ND (1.2)
1469-TCDD	2.4 (0.9)	ND (2.6)	ND (1.1)	8.9 (2.5)	1.0 (1.0)	1.4 (0.7)	ND (2.1)
1269-TCDD	6.6 (0.9)	9.0 (2.6)	2.6 (1.1)	16	3.8 (1.0)	12	ND (2.1)
1267-TCDD	3.0 (0.9)	5.5 (2.6)	1.4 (1.1)	5.4 (1.5)	2.2 (1.0)	7.0	ND (2.1)
1289-TCDD	4.3 (0.9)	7.1 (2.6)	2.2 (1.1)	5.9 (1.5)	3.0 (1.0)	10	ND (2.1)
1369-TCDD	9.5 (1.6)	8.1 (2.1)	3.0 (1.1)	64	5.2 (1.1)	15	ND (1.4)
1247 + 1248-TCDDs	13 (1.6)	16 (2.1)	10 (1.1)	46	11	59	ND (1.4)
1278-TCDD	10 (1.6)	11 (2.1)	4.6 (1.1)	33	9.2 (1.1)	35	ND (1.4)
1268-TCDD	11 (1.6)	11 (2.1)	4.2 (1.1)	41	9.4 (1.1)	39	ND (1.4)
1237 + 1238-TCDDs	18	18 (2.1)	8.0 (1.1)	39	16	69	ND (1.4)
1279-TCDD	15 (1.6)	21	6.8 (1.1)	52	11	48	ND (1.4)
"1246"-TCDD[b]	4.3 (0.9)	5.6 (1.8)	4.6 (0.9)	20	3.2 (0.8)	8.7 (1.0)	ND (1.4)
1478-TCDD	5.4 (0.9)	8.2 (1.8)	5.9 (0.9)	31	4.4 (0.8)	8.6 (1.0)	ND (1.4)
1236-TCDD	3.9 (0.9)	8.1 (1.8)	4.1 (0.9)	14	4.1 (0.8)	11	ND (1.4)
1239-TCDD	5.4 (0.9)	8.4 (1.8)	4.3 (0.9)	15	4.1 (0.8)	11	ND (1.4)
"1249"-TCDD[b]	3.5 (1.4)	7.7 (3.2)	9.1 (1.4)	20 (2.5)	4.4 (0.8)	25	ND (1.4)
1368-TCDD	18	15 (2.1)	4.6 (0.9)	23	15	24	ND (1.8)
1379-TCDD	14	12 (2.1)	3.8 (0.9)	25	9.7 (1.3)	20	ND (1.8)
1378-TCDD	11	24	6.2 (0.9)	31	19	46	ND (1.8)
1234-TCDD	2.7 (0.8)	7.1 (2.1)	1.5 (0.9)	5.7 (1.6)	1.6 (1.3)	1.5 (1.3)	ND (1.8)
total TCDDs	169	220.8	93.3	513.9	146.5	471.2	ND
isomers obsd	20	19	19	20	20	20	0
^{13}C-HCDD recovery	68%	61%	105%	100%	-[e]	-[e]	INT[f]
124679 + 124689-HCDDs	290	490	220	560	770	1100	ND (7.4)
123468-HCDD	91	74 (33)	32	190	70 (17)	30 (20)	ND (7.4)
123679 + 123689-HCDDs	590	2800	1400	640	5100	6300	ND (7.4)
123469-HCDD	ND[d] (30)	ND (65)	ND (35)	70	ND (70)	ND (200)	ND (7.4)
123478 + 123678-HCDDs	150	620	210	180	770	1200	ND (7.4)
123467 + 123789-HCDDs	130	360	120	160	330	590	ND (7.4)
total HCDDs	1251	4344	1982	1800	7040	9220	ND
$\mathrm{H_7CDD}$ corr factor[c]	68%	69%	96%	100%	86%	86%	74%
1234679-$\mathrm{H_7CDD}$	1100	2600	390	2900	850	1700	ND (3.2
1234678-$\mathrm{H_7CDD}$	1400	3200	570	1400	950	2400	ND (3.2
total $\mathrm{H_7CDDs}$	2500	5800	960	4300	1800	4100	ND
^{13}C-OCDD recovery	69%	77%	88%	100%	71%	72%	79%
OCDD	2400	5200	870	3200	1200	490	4.7 (4.7)

[a,b,c,d] Refer to Table I. [e] Indicates that the internal standard could not be quantitated because of the dilution necessitated by the high native CDD concentration. [f] A coeluting interference made quantitation of the ^{13}C-123478-HCDD internal standard impossible, for calculation purposes a 70% recovery is assumed.

TABLE III. C - CDDs in Parts per Trillion for Central Region RWC Unit Chimney Particulates

	central							
	no. 4	no. 97	no. 87	no. 56	no. 64	no. 81	reagent blank	Midland, MI[g]
chimney type	masonry	metal	metal	masonry	masonry	metal		masonry
sampling point	base	top	top	base	base	top		base
primary fuel	ash	birch	birch	birch	oak	birch		oak
operation[c]	low	low	low	low	low	high		low
^{13}C-2378-TCDD recovery	65%	NA[e]	68%	62%	69%	49%	62%	67%
2378-TCDD	20	NA	ND (1.3)	110	200	0.8 (0.7)	ND (2.4)	39
1469-TCDD	3.4 (2.2)	NA	ND (1.2)	31	28	ND (1.2)	ND (1.0)	7.5 (1.8)
1269-TCDD	9.8 (2.2)	NA	ND (1.2)	110	120	ND (1.2)	ND (1.0)	30
1267-TCDD	6.2 (2.2)	NA	ND (1.2)	53	66	ND (1.2)	ND (1.0)	21
1289-TCDD	6.6 (2.2)	NA	ND (1.2)	58	81	ND (1.2)	ND (1.0)	18
1369-TCDD	20 (2.3)	NA	ND (0.9)	260	170	ND (1.2)	ND (1.9)	49
1247 + 1248-TCDDs	43	NA	ND (0.9)	400	320	ND (1.2)	ND (1.9)	90
1378-TCDD	23	NA	ND (0.9)	260	220	ND (1.2)	ND (1.9)	55
1268-TCDD	23	NA	ND (0.9)	310	250	ND (1.2)	ND (1.9)	52
1237 + 1238-TCDDs	52	NA	ND (0.9)	500	330	ND (1.2)	ND (1.9)	75
1279-TCDD	18 (2.3)	NA	ND (0.9)	340	300	ND (1.2)	ND (1.9)	67
1246-TCDD[b]	8.9 (1.7)	NA	ND (0.7)	97	75	ND (1.2)	ND (1.9)	42
1478-TCDD	10 (1.7)	NA	ND (0.7)	120	100	ND (1.2)	ND (1.9)	21 (2.8)
1236-TCDD	11 (1.7)	NA	ND (0.7)	90	68	ND (1.2)	ND (1.9)	30
1239-TCDD	11 (1.7)	NA	ND (0.7)	100	80	ND (1.2)	ND (1.9)	36
1249-TCDD[b]	12 (2.6)	NA	ND (0.7)	97	140	ND (1.0)	ND (1.9)	15 (4.3)
1368-TCDD	110	NA	ND (1.0)	340	94	1.6 (1.0)	ND (2.3)	220
1379-TCDD	97	NA	ND (1.0)	270	130	1.4 (1.0)	ND (2.3)	150
1278-TCDD	57	NA	ND (1.0)	230	350	1.2 (1.0)	ND (2.3)	130
1234-TCDD	31	NA	ND (1.0)	55 (10)	23 (5.1)	ND (1.0)	ND (2.3)	22
total TCDDs	572.9	NA	ND	3831	3147	5.0	ND	1169.5
isomers obsd	20	NA	0	20	20	4	0	20
^{13}C-HCDD recovery	76%	77%	83%	–[f]	–[f]	71%	70%	–[f]
124679 + 124689-HCDDs	660	11 (4.4)	1.3 (1.3)	3700	10000	ND (4.6)	ND (2.0)	700 (110)
123468-HCDD	370	4.4 (4.4)	ND (1.3)	2000	4000	ND (2.5)	ND (2.0)	140 (110)
123679 + 123689-HCDDs	1100	21 (4.4)	1.9 (1.3)	6500	37000	6.3 (2.5)	ND (2.0)	1300
123469-HCDD	ND[d] (90)	ND (4.4)	ND (1.3)	400	ND (2000)	ND (2.5)	ND (2.0)	110 (110)
123478 + 123678-HCDDs	280	6.5 (4.4)	ND (1.3)	2700	8000	ND (2.5)	ND (2.0)	540 (110)
123467 + 123789-HCDDs	290	5.5 (4.4)	ND (1.3)	2100	6300	ND (2.5)	ND (2.0)	350 (110)
total HCDDs	2700	48.4	3.2	17400	65300	6.3	ND	3140
H$_7$CDD corr factor[c]	78%	72%	71%	100%	100%	86%	68%	96%
1234679-H$_7$CDD	5600	40	6.2	13000	20000	13 (1.9)	ND (1.6)	4000
1234678-H$_7$CDD	5900	40	6.3	12000	19000	13 (1.9)	ND (1.6)	3500
total H$_7$CDDs	11500	80	12.5	25000	39000	26	ND	7500
^{13}C-OCDD recovery	80%	67%	59%	–[f]	–[f]	100%	66%	88%
OCDD	15400	110	24 (2.5)	37000	30000	32 (5.2)	3.9 (3.0)	10600

[a,b,c,d] Refer to Table I. [e] Not analyzed, severe polyolefin interference. [f] Refer to footnote e in Table II [g] Preliminary experimental RWC unit chimney particulates sample from Midland, MI.

TABLE III. D - CDD Fortification and Recovery Data for RWC Unit Chimney Particulates

	added and found concn, pptr					
	low spike: 10.0 g central no. 87			high spike: 10.0 g eastern no. 1		
CDD isomers	added	found	% recovery	added	found	% recovery
^{13}C-2378-TCDD int std	5000	3630	72.6	5000	3260	65.3
2378-TCDD	15	10.8	72	100	64	64
1469-TCDD	15	9.6	64	100	68	68
1269-TCDD	15	10.5	70	100	74	74
1267-TCDD	15	11.1	74	100	76	76
1289-TCDD	15	7.4	49	100	73	73
1369-TCDD	15	12.4	83	100	67	67
1247 + 1248-TCDDs	30	23.1	77	200	124	62
1278-TCDD	15	10.8	72	100	61	61
1268-TCDD	15	10.8	72	100	63	63
1237 + 1238-TCDDs	30	26.4	88	200	132	66
1279-TCDD	15	11.8	79	100	64	64
1246-TCDD[a]	15	14.7	98	100	85	85
1478-TCDD	15	13.5	90	100	78	78
1236-TCDD	15	12.0	80	100	72	72
1239-TCDD	15	12.3	82	100	79	79
1249-TCDD[a]	15	11.7	78	100	90	90
1368-TCDD	15	10.4	69	100	69	69
1379-TCDD	15	11.2	75	100	86	86
1378-TCDD	15	11.7	78	100	82	82
1234-TCDD	15	11.1	74	100	91	91
mean recovery			76.2%			73.5%
std dev			10.1%			9.5%
^{13}C-HCDD int std	1000	820	82.0	1000	910	91.0
124679 + 124689-HCDDs	40	36.8	92	400	340	85
123468-HCDD	20	17.2	86	200	180	90
123679 + 123689-HCDDs	40	36.4	91	400	352	88
123469-HCDD	20	18.8	94	200	184	92
123478 + 123678-HCDDs	40	37.6	94	400	360	90
123467 + 123789-HCDDs	40	31.2	78	400	344	86
mean recovery			89.2%			88.5%
std dev			6.2%			2.7%
1234679-H$_7$CDD	31	-[b]	-	1240	1150[c]	93
1234678-H$_7$CDD	33	-	-	1320	1150[c]	87
mean recovery			-			90.0 %
^{13}C-OCDD int std	5000	4650	93.0	5000	4000	80.0
OCDD	200	178[c]	89	6000	4800[c]	80

[a] May be either 1246- or 1249-TCDD. [b] Fraction lost, see text. [c] Corrected for sample content.

TABLE III. E - Average CDD Concentrations in Parts per Trillion for RWC Unit Chimney Particulates[a]

	eastern	central	western	all regional samples
total TCDDs	2000	1500[b]	270	1200
total HCDDs	2200	14000	4300	6900
total H_7CDDs	2100	13000	3200	6000
OCDD	2000	14000	2200	6000
av total CDDs	8300	42500	9970	20100

[a] "Not detected" samples were calculated as zero.

[b] TCDDs for 5 samples, see Table III.

TABLE IV

OBSERVED CDD CONCENTRATIONS IN MILWAUKEE MILORGANITE SAMPLES

CDD Isomers	Observed Concentration in Parts per Trillion 1933 Milorganite	 1981 Milorganite	 1982 Milorganite
2378-TCDD	2.2 (0.8)+	11	16
1469-TCDD	ND$^{\#}$ (0.6)	ND (0.7)	ND (0.7)
1269-TCDD	ND (0.6)	ND (0.7)	ND (0.7)
1267-TCDD	ND (0.6)	ND (0.7)	ND (0.7)
1289-TCDD	ND (0.6)	ND (0.7)	ND (0.7)
1369-TCDD	1.4 (0.4)	1.4 (0.6)	3.4 (0.7)
1247+1248-TCDDs	4.8	1.4 (0.6)	3.2 (0.7)
1278-TCDD	1.4 (0.4)	2.2 (0.6)	3.0 (0.7)
1268-TCDD	1.4 (0.4)	1.1 (0.6)	2.4 (0.7)
1237+1238-TCDDs	2.2 (0.4)	93	140
1279-TCDD	1.6 (0.4)	1.4 (0.6)	3.4 (0.7)
1246-TCDD	ND (0.4)	ND (0.6)	ND (0.7)
1478-TCDD	0.8 (0.4)	0.8 (0.6)	2.0 (0.7)
1236-TCDD	ND (0.4)	ND (0.6)	ND (0.7)
1239-TCDD	ND (0.4)	ND (0.6)	ND (0.7)
1249-TCDD	ND (0.9)	ND (0.7)	ND (0.8)
1368-TCDD	7.2	9.2	15
1379-TCDD	3.5 (0.6)	6.0	12
1378-TCDD	5.5 (0.6)	10	22
1234-TCDD	1.8 (0.6)	ND (0.6)	ND (1.1)
Total TCDDs	33.8	137.5	222.4

TABLE IV

(continued)

OBSERVED CDD CONCENTRATIONS IN MILWAUKEE MILORGANITE SAMPLES

	Observed Concentration in Parts per Trillion		
CDD Isomers	1933 Milorganite	1981 Milorganite	1962 Milorganite
124679+124689-HCDDs	350	340	420
123468-HCDD	72	72 (18)	100
123679+123689-HCDDs	650	710	620
123469-HCDD	ND (32)	ND (18)	ND (14)
123478-HCDD	22 (3.0)	ND (18)	15 (5.7)
123678-HCDD	280	220	200
123467+123789-HCDDs	83	70 (18)	73
Total HCDDs	1457	1412	1428
1234679-H_7CDD	5000	4600	4000
1234678-H_7CDD	4700	4800	3600
Total H_7CDDs	9700	9400	7600
OCDD	59,000	50,000	60,000

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*May be either 1246- or 1249-TCDD. (+) Value in parentheses is limit of detection which is defined as 2.5 x peak to valley noise in an adjacent region of the mass chromatogram; if the limit of detection is less than 10% of the observed signal, it is not reported. (ND) Not detected at specified limit of detection.

TABLE V

VOLCANIC PARTICULATE EFFLUENT

Sample Identification	Distance and Direction From Volcano	Exposure Time in Days Following May 18, 1980 Eruption
Blast Zone		
#53 Blast Debris (Unit A)	~ 3 mi. NW, Studebaker Ridge	23
#50 Hot Ash (Unit C)	~ 5 mi. N, west of Spirit Lake	23
Rural Zones		
#58 Gifford Pinchot Nat. Forest (~3 mi. S. of Packwood, WA)	~ 40 mi. NE	17
#42 Yakima Canyon, WA (~17 mi. S. of Ellensburg, WA)	~ 85 mi. ENE	15
#86 Washtucna, WA (~2 mi. W. of Village)	~ 190 mi. E	24
#22 Moscow, ID (~20 mi. N. of City)	~ 250 mi. E	24
Interstate Highway Zones		
#27 Castle Rock, WA ~2 mi. east (~50 m W. of I-5)	~ 50 mi. W	10
#29 Ritzville, WA ~ 1 mi. east (~500 m NW of I-90)	~190 mi. ENE	14
#31 Spokane, WA ~ 10 mi. [illegible] (~100 m NW of I-90)	~ 240 mi. ENE	14
Urban Zones		
#40 Yakima, WA (near US-97 in City)	~ 90 mi. NE	15
#38 Ellensburg, WA (Central portion of City)	~ 100 mi. ENE	14
#26 Portland, OR (Northern portion of City)	~ 45 mi. SSW	11

TABLE VI

CDD CONTENT OF VOLCANIC PARTICULATES

Sample[a]	TCDD	HCDD	H_7CDD	OCDD	Total
Blast Zone					
#53 Blast Debris	ND(0.3)	ND(0.7)	0.8(0.3)	ND(1.6)	0.8
Rural Zones					
#58 Gifford Pinchot	ND(1.3)	ND(2.0)	ND(1.0)	ND(2.0)	ND
#42 Yakima Canyon	ND(0.3)	ND(0.8)	1.0(0.4)	3.2(1.6)	4.2
#86 Washtucna, WA	--[a]	ND(0.9)	ND(0.5)	ND(1.6)	ND
#22 Moscow, ID	--	ND(0.8)	ND(0.4)	ND(1.6)	ND
Interstate Zones					
#27 Castle Rock, WA	ND(0.9)	ND(2.0)	2.0(0.7)	6.0(1.6)	8.0
#29 Ritzville, WA	--	ND(0.8)	ND(0.5)	ND(1.8)	ND
#31 Spokane, WA	ND(1.6)	ND(2.0)	ND(1.0)	7.0(2.0)	7.0
Urban Zones					
#40 Yakima, WA	ND(0.2)	ND(0.4)	4.7	23	27.7
#38 Ellensburg, WA	ND(0.3)	ND(0.9)	2.6(0.4)	7.8	10.4
#26 Portland, OR	0.8(0.3)	22(0.9)	58(7.0)	170	250

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[a] --- Indicates that the sample was not analyzed for the specified component.

TABLE VI

(Continued)

PCB CONTENT OF VOLCANIC PARTICULATES

Sample	Total of Monitored PCBs (ppb)[a]
Blast Zone	
#53 Blast Debris	ND (20-170)
#50 Hot Ash	ND (20-180)
Rural Zones	
#58 Gifford Pinchot Nat. Forest	50
Interstate Highway Zones	
#27 Castle Rock, WA	40
#31 Spokane, WA	140
Urban Zones	
#40 Yakima, WA	1200

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[a] Penta-, hexa-, and heptachlorobiphenyls were determined.

TABLE VII

TCDD Isomer	Concentration (Parts per Trillion = pg/g)									
	Duluth-EPA Fly Ash (2.0g sample)		Reagent Blank (assume: 2.0g)		Exposure Fish A (25.0g)		Exposure Fish C (25.0g)		Reagent Blank (Assume 25.0g)	
		Rel.%		Rel.%		Rel.%		Rel.%		Rel.%
^{13}C-2378-TCDD % Recovery	76%		65%		80%		72%		70%	
2378-TCDD	160	0.48%	nd (3.1)		0.4 (0.2)	66.7%	70	84.2%	nd (0.2)	
1469-TCDD	42	0.13%	nd (4.2)		nd (0.2)		nd (0.2)		nd (0.2)	
1269-TCDD	140	0.42%	nd (4.2)		nd (0.2)		nd (0.2)		nd (0.2)	
1267-TCDD	65	0.20%	nd (4.2)		nd (0.2)		nd (0.2)		nd (0.2)	
1289-TCDD	55	0.17%	nd (4.2)		nd (0.2)		nd (0.2)		nd (0.2)	
1369-TCDD	740	2.24%	nd (3.4)		nd (0.2)		0.8 (0.3)	1.0%	nd (0.3)	
1247 + 1248-TCDDs	1700	5.15%	nd (3.4)		nd (0.2)		1.0 (0.3)	1.2%	nd (0.3)	
1278-TCDD	650	1.97%	nd (3.4)		nd (0.2)		0.6 (0.3)	0.7%	nd (0.3)	
1258-TCDD	760	2.30%	nd (3.4)		nd (0.2)		0.5 (0.3)	0.6%	nd (0.3)	
1237 + 1238-TCDDs	2700	8.17%	nd (3.4)		nd (0.2)		1.9 (0.3)	2.3%	nd (0.3)	
1279-TCDD	210	0.64%	nd (3.4)		nd (0.2)		0.3 (0.3)	0.4%	nd (0.3)	
1246/1249-TCDD (1.328)	160	0.48%	nd (3.4)		nd (0.2)		0.2 (0.1)	0.2%	nd (0.3)	
1478-TCDD	140	0.42%	nd (3.4)		nd (0.2)		0.1 (0.1)	0.1%	nd (0.3)	
1236-TCDD	220	0.67%	nd (3.4)		nd (0.2)		0.2 (0.1)	0.2%	nd (0.3)	
1239-TCDD	190	0.58%	nd (3.4)		nd (0.2)		0.2 (0.1)	0.2%	nd (0.3)	
1246/1249-TCDD (1.411)	160	0.48%	nd (3.4)		nd (0.3)		0.3 (0.2)	0.4%	nd (0.3)	
1368-TCDD	13000	39.3%	nd (2.2)		0.2(0.1)	33.3%	3.9	4.7%	nd (0.2)	
1379-TCDD	9800	29.7%	nd (2.2)		nd (0.1)		1.9 (0.2)	2.3%	nd (0.2)	
1378-TCDD	1700	5.15%	nd (2.2)		nd (0.1)		1.2 (0.2)	1.4%	nd (0.2)	
1234-TCDD	440 (80)	1.33%	nd (2.2)		nd (0.1)		nd (0.2)		nd (0.2)	
Total TCDDs	33032	99.9%	nd		0.6	100%	83.1	99.9%	nd	
		Rel.%		Rel.%		Rel.%		Rel.%		Rel.%
HCDD										
^{13}C-123478-HCDD % Recovery	native too large		98%		Interference		native too large		90%	
124679 + 124689-HCDDs	8800	8.5%	nd (13)		nd (0.5)		<20 (Int.)		nd (0.4)	
123468-HCDD	46000	44.3%	nd (13)		0.7 (0.5)		36 (10)		nd (0.4)	
123679 + 123689-HCDDs	30000	28.9%	nd (13)		0.8 (0.5)		40 (10)		nd (0.4)	
123469-HCDD	nd (1800)	—	nd (13)		nd (0.5)		nd (10)		nd (0.4)	
123478 + 123678-HCDDs	11000	10.6%	nd (13)		1.8 (0.5)		820		nd (0.4)	
123467 + 123789-HCDDs	8000	7.7%	nd (13)		0.8 (0.5)		270		nd (0.4)	
Total HCDDs	103800	100%	nd		4.1		1166		nd	

TABLE VII

(continued)

Concentration (Parts per Trillion = pg/g)

	Duluth-EPA Fly Ash (2.0g sample)		Reagent Blank (assume: 2.0g)		Exposure Fish A (25.0g)		Exposure Fish C (25.0g)		Reagent Blank (Assume 25.0g)	
		Rel.%		Rel.%		Rel.%		Rel.%		Rel.%
H_7CDD										
1234679-H_7CDD	36000	46.2%	nd (14)		2.8 (1 [illegible]		100		nd (0.8)	
1234678-H_7CDD	42000	53.8%	nd (14)		5.3 (1.0)		2000		nd (0.8)	
Total H_7CDDs	78000	100%	nd		8.1		2100		nd	
OCDD										
^{13}C-OCDD % Recovery	native too large		90%		99%		native too large		79%	
OCDD	5200	100%	nd (29)		6.6 (1.2)		1100		nd (2.3)	

Mr. SCHEUER. Does that complete your testimony?

Mr. BUZZELLI. Yes, it does, Mr. Chairman.

Mr. SCHEUER. Mr. Buzzelli, when was the last time that the Dow executives or scientists contacted the EPA scientists regarding the draft report that you discussed?

Mr. BUZZELLI. To my knowledge, sir, the last time there was any contact was in the telephone conversation that I mentioned in my testimony with region V, the telephone call between myself, Dr. Kagel from Dow, and Dr. Clark and Mr. Kee from region V.

Mr. SCHEUER. Did you testify before that you were invited to submit comments on that report? I know the president of Dow Chemical remarked on television a few days ago that the Dow Chemical Co. was invited to submit their comments and scientific critique of that report. Is that your statement, too?

Mr. BUZZELLI. We received a copy of the report and were told to submit our comments directly to the author in region V. We did treat it as a scientific review, sir.

Mr. SCHEUER. You received a copy of the report?

Mr. BUZZELLI. Yes, sir.

Mr. SCHEUER. How did that happen?

Mr. BUZZELLI. As best as we can reconstruct, sir, we got that copy from the EPA headquarters in Washington.

Mr. SCHEUER. That was in response to what?

Mr. BUZZELLI. That was in response to our inquiries to the EPA headquarters in Washington on the report's existence following the publishing of portions of the report in the Toronto Globe and Mail.

Mr. SCHEUER. Did you ask to see the report?

Mr. BUZZELLI. We called region V—rather, we called EPA headquarters or contacted them and asked what the report was about.

Mr. SCHEUER. Did you ask to see the report?

Mr. BUZZELLI. I personally did not, sir. I do not know anybody that personally asked to see the report in Dow.

Mr. SCHEUER. Then why was the report sent to you?

Mr. BUZZELLI. I can't answer that, sir, since I was not the sender; I was only the receiver.

Mr. SCHEUER. Your president, I heard on television, commented that they were invited to comment on the report. Is that consistent with your knowledge of events?

Mr. BUZZELLI. We received the report and were told to give our comments to the——

Mr. SCHEUER. Who told you that?

Mr. BUZZELLI. Somebody in EPA headquarters in Washington.

Mr. SCHEUER. Who?

Mr. BUZZELLI. I don't know specifically.

Mr. SCHEUER. Somebody in EPA headquarters in Washington told you to give your comments——

Mr. BUZZELLI. Told our Washington office.

Mr. SCHEUER. And you don't know who that was?

Mr. BUZZELLI. No, sir, I do not.

Mr. SCHEUER. Do you know who it was in the Washington office who was told by EPA to give their——

Mr. BUZZELLI. The report was received by a secretary in the Washington office.

Mr. SCHEUER. The secretary had the conversation with EPA?

Mr. BUZZELLI. The secretary apparently had conversations with somebody in the EPA, but I don't know——

Mr. SCHEUER. The EPA didn't have conversations with anybody at a higher professional level than a secretary when this request came for Dow to comment on that report?

Mr. BUZZELLI. Sir, I think we need to back up just a little bit. When we started getting the press involved, our Washington office contacted the Washington office——

Mr. SCHEUER. Who in your Washington office?

Mr. BUZZELLI. I do not——

Mr. SCHEUER. The Washington office is not a person; it is just a piece of real estate.

Mr. BUZZELLI. It is a group of people, sir.

Mr. SCHEUER. Who residing in your Washington office?

Mr. BUZZELLI. I do not know who.

Mr. SCHEUER. Would you find out who and let us know? We will keep the record open for a few days for you to do that.

Mr. BUZZELLI. Mr. Chairman, I have tried to find out who and the people involved. I was put in charge of looking into this by my company, and I have not been able to reconstruct this event, which happened almost 2 years ago, in terms of the particulars. I can give you accurate knowledge of my involvement of it. I have attempted to reconstruct what happened.

Mr. SCHEUER. What I am trying to suggest, Mr. Buzzelli, is that this is an extraordinarily unusual situation. We are quite familiar with the peer review process, and so are you. The peer review process is a very useful process. The peer review process makes possible the contribution of the wisdom and the knowledge and the very sophisticated scientific capability of the private sector, but it comes at a proper time according to a proper process. It comes after the scientists have finished their work and feel that their scientific study now is ready for commentary by the greater scientific community, including the corporate community, whose contributions over the years have been very significant, very worthwhile, very positive.

But, what we have here, Mr. Buzzelli, is an intervention and, to the best of our knowledge, we cannot find any EPA official who invited Dow to make this contribution. We find that Dow requested the document and requested the opportunity to make suggestions for deletions and changes in phraseology in this report before it was completed by the scientists, before the scientists were ready to declare it their own.

This is what is very unusual about this case. This is not a normal, conventional case of a corporation making its contribution as part of the peer review process. This is a corporation gratuitously intervening on its own demand or its own request before the scientific report was finished to censor, delete, and change phraseology of the scientists' wording of the scientists' report before they were finished with it. As a matter of fact, the regional office in Chicago, as you know, was told by the EPA that they would not give them permission to release that report until these changes were made. Now I do not hold that to be Dow's responsibility; that is the responsibility of EPA Washington headquarters, but I am concerned that there is a grave misunderstanding in the land about how this intervention took place.

To the best of my knowledge, and I want you to correct me if you can, no EPA official ever invited Dow to make this intervention. Dow requested to see the report and Dow requested the opportunity to make suggestions, deletions, changes, and alterations in this scientific report while it was being formulated but before it had been finalized and before it was ready for the normal, conventional peer review process.

Mr. BUZZELLI. Mr. Chairman, you did invite to make comments——

Mr. SCHEUER. Please do, yes.

Mr. BUZZELLI [continuing]. If I didn't agree with you, and I am sorry, sir, I do not.

We simply made an inquiry to the EPA to find out what the report was all about because it was——

Mr. SCHEUER. You asked to see the report?

Mr. BUZZELLI. To find out was there a report, because it was being printed in the Toronto Globe and Mail and other newspapers, and we were getting inquiries. We made an inquiry to the EPA. I cannot track down the details for you, Mr. Chairman. I wish I could. However, the next event that I have been able to reconstruct is that a copy of the report came from EPA headquarters to Dow asking us to pass any comments on to region V directly to the author. I do not know of anybody in the Dow Chemical Co. that asked for the opportunity to review the report and asked for the opportunity to give our comments.

We reviewed it and we——

Mr. SCHEUER. Do you know anybody in EPA who requested Dow kindly to make their contribution or their comments on that report while it was still in the process of formulation by the scientists before it had been finalized?

Mr. BUZZELLI. Do I—I am sorry, sir. Would you repeat the question?

Mr. SCHEUER. Do you know who in EPA requested Dow to make their contribution? This is what your president said.

Mr. BUZZELLI. No, I do not, sir.

Mr. SCHEUER. OK. In an article that was published in the October 24, 1980, issue of Science magazine entitled, "Trace Chemistries of Fire: A Source of Chlorinated Dioxins," which was published, as I said, on October 24, 1980, they provided five samples of dioxin contamination as high as 100 parts per billion. Do you know the exact location—I take it you are familiar with that article which I assume was written by Dow scientists?

Mr. BUZZELLI. Yes, I am, Mr. Chairman.

Mr. SCHEUER. You are familiar with it?

Mr. BUZZELLI. Yes.

Mr. SCHEUER. OK. Do you know the exact location of the five samples in which dioxin contamination was found?

Mr. BUZZELLI. I do not know the precise location, but I know within a fairly close proximity of where they were, sir.

Mr. SCHEUER. Were they in Midland, inside the Dow plant?

Mr. BUZZELLI. Yes, sir.

Mr. SCHEUER. OK. Do you know how scientifically accurate the analysis of these samples was at that time?

Mr. BUZZELLI. Dr. Bumb, would you care to comment?

Mr. SCHEUER. Just briefly.

Dr. BUMB. Those samples were 8 to 10 times the signal-to-noise ratio. Therefore, they are an accurate number, sir.

Mr. BUZZELLI. Mr. Chairman, with regard to the sample locations, they were inside of our facility and they were very close to our powerhouse and our incinerator.

Mr. SCHEUER. Right. Has anybody other than Dow scientists ever analyzed the soil in and around the Dow plant for dioxin contamination?

Mr. BUZZELLI. I don't know of anybody that's analyzed it, but around the Dow plant——

Mr. SCHEUER. Inside the Dow plant.

Mr. BUZZELLI. Not to my knowledge, sir.

Mr. SCHEUER. Would you have any objection if the EPA or the Center for Disease Control in Atlanta were to ask access to the plant so that they could collect and analyze soil samples around the plant, inside the plant property?

Mr. BUZZELLI. I think that is a hypothetical question, but let me try to answer it.

Mr. SCHEUER. Well, let's assume a question like that could come down the pike one of these days.

Mr. BUZZELLI. Yes, it certainly could.

I think it depends a little bit on what the purpose of the study is, sir, and particularly the science involved and whether a protocol is written, and then we would sit down and certainly be glad to discuss it with any agency.

Mr. SCHEUER. Let me be a little more specific.

I presume that if EPA, under its excellent new leadership, or the Center for Disease Control, or both, were to suggest to you that they would like to make some scientific samples of the soil in the Dow plant, as well as in other places in Midland, that they would be doing so subject to a professional plan and a professional regiment. Would you have any objection to their proceeding with this research?

Mr. BUZZELLI. We would certainly welcome the opportunity to sit down with them, Mr. Chairman, but until we sit down with them and discuss the research and the protocol and the science involved, I simply cannot answer the question. But, we certainly welcome the opportunity to sit down and discuss it, the details.

Mr. SCHEUER. Now, look, let's go a little beyond sitting down and discussing the details. Let us assume that they have produced a scientifically and professionally adequate protocol. Let's assume that. OK? I assume that the EPA and the Center for Disease Control would know how to produce a satisfactory protocol for that research.

Assuming that, would you have any objection to their coming inside the outside perimeter, the gates of the Dow Chemical Co., and doing an analysis of your soil that presumably presents the possibility of dioxin contamination?

Mr. BUZZELLI. I think that providing that our process technology was also protected in this study that you are talking about, which is always of concern to us, and the fact that we were in agreement on the protocol and understood the protocol, I assume that we would let them in the plant, sir, but I can't give a yes or no answer until——

Mr. **Scheuer**. If they were to take soil samples—pardon?

Mr. **Buzzelli**. I cannot give you an absolute yes or no answer until the event actually takes place, Mr. Chairman.

Mr. **Scheuer**. Assuming that protocol was proper, is there anything about the fact of their collecting soil samples for analysis that would have any impact on your product, on your proprietary—on the proprietary aspects of your production, merely collecting a sample of soil?

Mr. **Buzzelli**. No, certainly not collecting a sample.

Mr. **Scheuer**. OK. Then there would be no objection, assuming that the protocol was adequate? I am trying to pin you down, Mr. Dow—Mr. Buzzelli, because I think that——

Mr. **Buzzelli**. You are making me feel like Mr. Dow.

Mr. **Scheuer**. Yes. Forgive me for institutionalizing you.

I think it is highly likely that this subcommittee and other subcommittees are actually going to request——

Mr. **Buzzelli**. Yes, sir.

Mr. **Scheuer** [continuing]. The EPA and the Center for Disease Control to make such a study. We want to know. We think we need more knowledge than we have now

Mr. **Buzzelli**. I agree with that.

Mr. **Scheuer**. Your position—of course, you do. Your position is that dioxin is benign to human beings and that ever since man first broiled the first steak a million years ago, we have been producing dioxin and that is a fact of life, part of our environment. In modest concentrations it may be harmful to fish and laboratory animals, but as far as man is concerned, it presents no health—no serious health problems. Isn't that more or less Dow's position?

Mr. **Buzzelli**. Mr. Chairman, let me see if I can get this back into perspective.

We did not say that dioxin was benign ever.

Mr. **Scheuer**. What is your position on its effect on human health in high concentrations?

Dr. **Gehring**. I am sorry, I was talking here about another question. Could you repeat your question again?

Mr. **Scheuer**. Yes. Here's my question: We are faced with a very sensitive and delicate problem here today. We are not trying to demagogue this problem. We are trying to be as thoughtful and as moderate and as considerate as we can. We are not trying to aggravate people's fears.

We do not have absolute knowledge that dioxin, even in high concentrations, is dangerous to human health. You have stated that in the kind of concentrations that we have all over the place that it is part of our environment; it comes from incinerators; it comes from woodburning stoves; it comes from cooking charcoal steak in your backyard. It is part of the facts of life, and there seems to be no serious threat to human health.

Am I putting words in your mouth or is that more or less Dow's position?

Dr. GEHRING. You are putting words in my mouth to some degree. When you say "high concentrations," obviously when you get sufficient high concentrations of dioxin, it could be, and indeed has been, hazardous to human health. There have been explosions in which there have been severe contaminations. Under those conditions, it surely is hazardous to human health.

Mr. SCHEUER. In what way?

Dr. GEHRING. As I indicated, the sentinel of dioxin intoxication is chloracne. At that point that is not a systemic disease, or we do not even know that totally. But, it is a disfiguring disease.

It does go to the point where we have had liver toxicity and we have had systemic disease, nausea, vomiting, and that sort of thing.

Mr. SCHEUER. Kidney problems?

Dr. GEHRING. Yes, certainly.

Mr. SCHEUER. Liver problems?

Dr. GEHRING. Yes.

Mr. SCHEUER. At what level of concentration? How many parts per billion?

Dr. GEHRING. In those cases where we know that those kinds of effects have occurred—for example, at least in the literature, in the horse arena in Missouri they had about 21 parts per million in that soil, 21 parts per million.

In the case of Seveso, the estimate is that they had 15 parts per million on the foilage, so it was much more available on the foilage than it was in the dirt. One of the properties of dioxin, which is important from the standpoint of human exposure or exposure of anything, is the fact that it binds very tenaciously to soil, which precludes its movement out into the environment but also precludes its movement through the skin into the body.

Mr. SCHEUER. Right. Let's get back to the original question I asked Mr. Buzzelli.

Assuming that EPA and the Center for Disease Control in Atlanta came up with a proper professional protocol, would you see any objection to their being permitted to examine soil samples within the Dow plant?

Mr. BUZZELLI. I would not, sir. I would like to add, Mr. Chairman, that last week we repeated the sampling of the soil samples in the plant that were reported in 1978 in the city of Midland and in the other communities where those soil samples were taken. We have already taken the samples, and are in the process of taking the samples outside of the city of Midland, repeating exactly the protocol that was followed in our 1978 report. Those samples are taken from Midland. They are being taken outside of Midland now.

Dr. GEHRING. Mr. Chairman, may I add one thing?

Mr. SCHEUER. Sure.

Dr. GEHRING. I feel, because of the ubiquitousness of this material in the environment, such a study would certainly include, I am sure you will concur, that sampling in other areas, industrialized areas, places of combustion, and so on, to provide perspective overall.

Mr. SCHEUER. Absolutely. Absolutely.

Presumably, it would include a study of a new Government property about to be acquired called Times Beach, Mo., and other places that you probably would want to suggest.

Let me ask Mr. Buzzelli, in connection with who generated the request to EPA to give them that study—did you check with Mr. Sercu?

Mr. BUZZELLI. Yes, I did, sir. He did not specifically remember.

Mr. SCHEUER. He does not specifically remember. Did he say he didn't?

Mr. BUZZELLI. No, sir, he did not.

Mr. SCHEUER. Let me say that this is a very perplexing issue. It is rather similar in nature to the problem of acid rain, that has not shown devastating health effects on humans. It has had devastating effects on crops; on grasslands; on forests, particularly forests in Canada; on lakes; on streams; on fishlife, particularly in Canada but also throughout the eastern coast of the United States; devastated the Adirondack lakes, about half of them cannot sustain fishlife.

In our efforts to apply some kind of regulatory approach, industry has responded saying, "You don't know everything. Therefore, you can't do anything."

It is true, we don't know everything about acid rain. The whole business of transport of these particulates, the sulfur dioxide particulates in the air is an extraordinarily complicated business. We really do not know everything, and we cannot prove that a plant emitting pollution here, if you cut down the pollution 10 percent, it will result in a 10-percent reduction of polluting in the Adirondacks or in the forests and lakes of Canada. We have not established that linearity that would produce a firm and provable cause and effect between cutting down pollution here and the cutting down of polluting effects here.

Industry has generally said, since we do not know everything, we cannot do anything. You may justify that, if you wish, where human health is not involved, and it does not seem to be involved with acid rain. Almost everything else on our planet seems to be involved—the fish, the rivers, the lakes, the forests, the crops, the buildings, the structures themselves are all damaged, but human health seems to be less damaged.

Here, on the question of dioxin, when you say since you cannot prove human health, damage to human health with the most toxic substance known to mankind in whatever concentrations, and because you cannot damage to human health in a poisonous, toxic substance that is 150,000 times more powerful than cyanide, because you cannot prove everything, you cannot do anything. That is a little touch for us to accept, and I think it is tough for the American people to accept.

We want to move prudently. We want to move responsibly. We are not interested in making charges and increasing the level of rhetoric so that people become anxiety ridden about this stuff that we know is there, but we are rappling to get some help with what we can do that would be useful and constructive and cost-effective in the present state of our knowledge.

Dr. GEHRING. Mr. Chairman, could I respond momentarily to that?

Mr. SCHEUER. Yes.

Dr. GEHRING. Perhaps this is a show of righteous indignation, but the fact is—for example, when we started producing 2,4,5-T back in

1950, very early we were doing samples to check for chloracne and minimizing the dioxin content of that product to such that it did not cause chloracne.

In our situation where we had the accident in 1964, we had an outbreak of chloracne. At that time we did not have the analytical techniques available to us now. We used again a rabbit ear bioassay to lower the concentrations and clean this up, so that our workforce would not be affected.

When I said "in righteous indignation," I assure you, sir, that we have been concerned about this for many, many years—in fact, years before we were being regulated for the material—and have tried to minimize this material in the product or in places where people would be exposed.

Mr. SCHEUER. I am sure you have.

I can also add, to give a little substance to my feeling of disquietude about your attitude that there is no visible, provable harm to humans of a life-threatening nature from dioxin and, therefore, you do not seem to feel the need for any regulation, in discussing this matter with the Center for Disease Control people they admit they do not know everything about dioxin. They feel unhappy about the current state of their knowledge, but they do say this: A decade ago in all the scientific appraisals of the various toxic substances in our country, viewed in the light of what we know today, we have vastly understated, we have vastly underestimated, the harmful effects of these toxic substances.

Therefore, they say today, "Don't underrate these matters because in the past, a decade ago, our appraisals vastly underrated the seriousness of the problem." It pays to be a little conservative. It pays to be a little prudent. It pays to go the extra mile to protect society from what might be, from what could be, in the way that we didn't do a decade ago.

Distinguished ranking minority member, Ray McGrath of New York?

Mr. MCGRATH. Thank you, Mr. Chairman.

We are going to have an opportunity to see how conservative you are this afternoon when we vote on the budget.

The testimony of Mr. Buzzelli—I am not going to get into the scientific rights or wrongs of this particular issue. I want to get into, if I may—to quote the former majority leader of the Senate a number of years ago, "When you knew about this thing and how you got into it"—your testimony is that somebody called you up on June 13, 1981, and asked you about an EPA report regarding your plant in Midland, Mich. It is your testimony that you knew nothing about that report at that time?

Mr. BUZZELLI. That is correct, sir.

Mr. MCGRATH. Did you immediately call the EPA region V headquarters—how soon after you found this out?

Mr. BUZZELLI. Sir, the phone call was not made to region V headquarters.

Mr. MCGRATH. Where was it made?

Mr. BUZZELLI. The phone call was made to the Washington office because at that point in time we did not know there was a region V report or any EPA report, for that matter.

Mr. McGRATH. Your testimony is that EPA headquarters at that time didn't seem to know that there was a report regarding your Midland plant; is that correct?

Mr. BUZZELLI. Yes, sir.

Mr. McGRATH. It says, on June 29, approximately 2 weeks—or 2½ weeks later—you received a copy of that?

Mr. BUZZELLI. Yes, sir.

Mr. McGRATH. That was dated June 18. In other words, sometime between June 13 and June 29 the EPA headquarters in Washington was made aware of a region V report regarding the Dow plant in Midland, Mich.?

Mr. BUZZELLI. I would assume that is correct.

Mr. McGRATH. Do you have any idea—could you tell me what date the conference call between Mr. Hernandez and Mr. Kagel occurred?

Mr. BUZZELLI. Would you repeat the question, sir?

Mr. McGRATH. The conference call between Mr. Hernandez and Mr. Kagel——

Mr. BUZZELLI. There was no conference call between Hernandez and Mr. Kagel.

Mr. McGRATH. There wasn't? Who called Mr. Hernandez regarding the change or suggested change in language of the report by Dow Co.?

Mr. BUZZELLI. I don't know of anybody from Dow Chemical that phoned Mr. Hernandez.

Mr. McGRATH. Do you know to whom Mr. Kagel spoke regarding the Dow recommendations to——

Mr. BUZZELLI. Within the EPA, sir? Is that your question?

Mr. McGRATH. Yes, sir.

Mr. BUZZELLI. Yes, sir. He spoke to Mr. David Kee and Dr. Milton Clark of region V. Dr. Clark was the author of the report.

Mr. McGRATH. Clark?

Mr. BUZZELLI. Clark.

Mr. McGRATH. It is your testimony that the recommendations made by the Dow Co. were miniscule, changing of words, semantics, regarding conclusions versus speculation; is that correct?

Mr. BUZZELLI. I made that statement, sir, about the one quote that has appeared in the hearings and in the newspaper. There were other changes that Dr. Kagel recommended to region V, also.

Mr. McGRATH. How extensive were those recommendations?

Mr. BUZZELLI. I cannot answer that question, except that the scientific review of the paper was done by Dr. Kagel as a thorough review of the paper.

Mr. McGRATH. I guess it is somebody from EPA—regarding the conference call between Mr. Kee, Mr. Clark—I guess these are Mr. Clark's notes—Mr. Kagel, and somebody else at Dow?

Mr. BUZZELLI. Yes, sir, I am aware of those.

Mr. McGRATH. Are you aware of the extent of the changes that were suggested at least by the notes of Mr. Clark?

Mr. BUZZELLI. I am aware that there were many suggested changes, sir.

Mr. McGRATH. It was not a mere changing of conclusions to speculation?

Mr. BUZZELLI. No, there was——

Mr. **McGrath**. There were substantive changes that were being suggested by Mr. Kagel to EPA officials?

Mr. **Buzzelli**. There were many recommended changes, including one of them was that the word "concluded" be changed to "speculate."

Mr. **McGrath**. Do you know how many of these recommendations for change were implemented in the final draft of the——

Mr. **Buzzelli**. I do not know how many recommended corrections there were to the report, sir.

Mr. **McGrath**. All of this began as an inquiry, a simple inquiry, from your company to the EPA to find out whether or not there was a report being done; is that correct?

Mr. **Buzzelli**. To the best of my knowledge, sir, yes, it is.

Mr. **McGrath**. I guess the rest of the questions I am going to have would be for the EPA.

Mr. **Scheuer**. Congressman Lewis?

Mr. **Lewis**. Mr. Buzzelli, in the January 5 issue of Chemical and Engineering News there was an article published. "Dow study finds 2,4,5-T no pregnancy risk." Was that study done by Dow scientists?

Mr. **Buzzelli**. If you may, sir, I might direct that question to Dr. Gehring. I am not familiar with the article from which you are quoting.

Dr. **Gehring**. I am not familiar with the article, either. Would you repeat the question?

Mr. **Lewis**. OK. On January 5, 1981, in the issue of Chemical and Engineering News there was an article published entitled, "Dow study finds 2,4,5-T no pregnancy risk." Was that study done by Dow scientists?

Dr. **Gehring**. I can't answer that. You said 1981?

Mr. **Lewis**. 1981.

Dr. **Gehring**. I suspect, without knowing, that that was in response to the Alsea, Oreg., study, but I am not sure.

Mr. **Lewis**. Does the——

Dr. **Gehring**. I would have to have more information than that to pinpoint what that article was. I do not know what the article was.

Mr. **Lewis**. If the article that was printed states, "Dow study finds no pregnancy risk"——

Dr. **Gehring**. Well, the reason I am hesitating is we have done numerous studies. We have done reproduction studies on 2,4,5-T in which the animals are exposed to the compound for three generations throughout pregnancy, throughout their growth, and so on. That is one.

We have done studies on teratology where you actually have pregnant females and you give them high doses of the compound to assess whether or not it will cause an abnormal effect. We have done that in two different species.

We have, in addition, done some additional evaluations, for example, in the case of the Alsea—did a study, as many other people did, to assess the validity of those data.

There are too many studies to pinpoint which one that was referring to.

Mr. **Lewis**. Let me ask you this, then: Has Dow done any study as far as pregnancy risks in relation to 2,4,5-T?

Dr. Gehring. Yes. Definitely. Those I just told you about.

Mr. Lewis. OK. I wanted you to say yes or no.

Dr. Gehring. Yes.

Mr. Lewis. Did you use the wives of employees at the Dow plant at Midland during the period of 1970 to 1975 for this type of a study? Can you recall the time period and whether it was done——

Dr. Gehring. No. What we did, we implemented a study of those exposed to potential dioxin contamination, the husbands, and we did do a study, a retrospective study, where we went back and through questionnaires asked the wives about their reproductive history. We have done that study, which has been published, sir.

Mr. Lewis. Is the Dow Midland plant—maybe this should be for Mr. Buzzelli—is the Dow plant in Midland currently manufacturing 2,4,5-T?

Mr. Buzzelli. At this point in time it is not, sir.

Mr. Lewis. Does that plant in Midland, Mich., currently emit dioxin?

Mr. Buzzelli. Because of the combustion sources we have present, I would assume so, that it is, but it would not be specifically—it may not be specific to the manufacture of chemicals but because we really do have a very, very large powerhouse and a rather large incinerator on the site.

Mr. Lewis. I have no further questions at this time, Mr. Chairman.

Mr. Scheuer. Congressman Chandler?

Mr. Chandler. To clarify, Mr. Buzzelli, your responses to Mr. McGrath, in your statement—I don't know whether you misled me or I simply misunderstood—you state regarding the statement that:

> Dow has been the primary contributor to contamination of the Tittabawassee River and Saginaw River and Lake Huron, it was our suggestion to region V that we simply change the word from "the EPA concludes" to "the EPA speculates."

Is that to say that is all that you suggested be changed in the report?

Mr. Buzzelli. No, sir. There were other corrections that we also made comments on or other areas that we made comments on.

Mr. Chandler. What was the tone of that conversation? Was this angry, combative, confrontive?

Mr. Buzzelli. No, sir. To the best of my recollection, I was on the telephone during part of the conversation, it was two professional people talking to each other. I noted no frustration or no anger.

Mr. Chandler. Dr. Kagel being the professional from Dow?

Mr. Buzzelli. And the people from region V, sir, also, I am speaking about.

Mr. Chandler. But you do not have any record or recall what other suggestions were made for changes in the report?

Mr. Buzzelli. I do not, sir.

Mr. Chandler. Was anyone else contacted about this report outside EPA, the White House, Members of Congress, by Dow people?

Mr. Buzzelli. To the best of my knowledge, Dow people, to my knowledge, did not contact anybody else about the report. To the best of my knowledge, at the end of the phone conversation with region V, that was the end of Dow's involvement in the report.

Mr. **Chandler**. This report hit when you learned of it from the press, which is a lousy way to learn of it——

Mr. **Buzzelli**. Yes, sir, it is.

Mr. **Chandler**. I agree. It had to be a big thing. This must have been a priority item, sort of stop the processes and let's deal with it. It must have been a big thing that was going on within that company.

Mr. **Buzzelli**. No, sir, I would not describe it as a big thing. We were getting phone calls on it. We were concerned about it. We were concerned about the accuracy of the statement, but we were concerned about quotes coming from a report that apparently concerned Dow that we had no knowledge of, but I do not want to leave you with the impression that a large number of people got involved. The proper people that worry about our environmental affairs, for example, were the people that got involved, as they normally would with any press inquiry.

Mr. **Chandler**. In your past dealings and in subsequent dealings with the Environmental Protection Agency, when a report of this kind is done on operations of your company, is it common procedure that you would see a draft statement of the report and have an opportunity to comment on that before it was made public?

Mr. **Buzzelli**. We have done reviews of EPA documents, sir, before they are published, yes, scientific peer reviews.

Mr. **Chandler**. But in this case that procedure apparently was not followed, even though that does appear to be——

Mr. **Buzzelli**. Well, it is the procedure, sir, that we followed. When we received the report, we treated the report as though it were a scientific review.

Mr. **Chandler**. I am sorry. You misunderstood me. In this case the report was in its fourth draft before you learned of it. Are there cases when the Environmental Protection Agency would have a report of this type on any of your operations in process and that they would provide that to you before that report was made final?

Mr. **Buzzelli**. I don't know the answer to the question, sir.

Mr. **Chandler**. Thank you, Mr. Chairman.

Mr. **McGrath**. Would the gentleman yield?

Mr. **Chandler**. Of course.

Mr. **McGrath**. Who did you call in the White House—or in EPA before—who did you call in EPA in Washington to find out whether or not there was a report available, an ongoing report?

Mr. **Buzzelli**. The EPA headquarters was called, sir. I don't know who specifically was called.

Mr. **McGrath**. Who do you normally deal with in Washington?

Mr. **Buzzelli**. I personally cannot answer that question, sir, because my responsibility is for Michigan, and I personally deal mostly with region V. I personally simply do not have the answer to your question.

Mr. **McGrath**. Would you characterize the nature and tone of the report before changes were made to be antagonistic toward your company or fair?

Mr. **Buzzelli**. Sir, the draft that we received—and apparently that is not the same draft that other people have been talking about—our concern from the draft that we saw was that the scientific conclusions were not correct.

Mr. **McGrath**. There were changes made based on recommendations which you have made?

Mr. **Buzzelli**. I do not know that, sir. The final version of the report is different than the draft that we received. I don't know who made the changes. I don't know who requested the changes.

Mr. **McGrath**. Would you characterize the final version of the report to be as antagonistic toward your company as the fourth draft?

Mr. **Buzzelli**. I would not characterize the two versions of the report as being different in attitude. I think they are different in science but not in attitude in terms of a significant difference.

Mr. **McGrath**. I have no further questions.

Mr. **Scheuer**. Did you talk to Paul Blair, the vice president of Dow, as to whether he had asked EPA about making changes in the report?

Mr. **Buzzelli**. I spoke with Dr. Etcyl Blair last Friday following Mr. Adamkus' testimony in front of Congressman Dingell's subcommittee. I did speak with him.

Mr. **Scheuer**. Congressman Torricelli of New Jersey?

Mr. **Torricelli**. Thank you, Mr. Chairman.

I would like to ask the question of dioxin from a slightly different perspective, not to the point of what Dow Chemical may or may not have been compelled to do, but I would like to ask you what you feel compelled to do. What at this point is Dow Chemical doing to determine the impacts of dioxin and what has been done?

Mr. **Buzzelli**. Since 1978, sir, since we first published the Trace Chemistries of Fire, we have continued to have ongoing dioxin research and have continued to publish quite a few papers. We do have an active research program in the area of dioxin, trying to understand more about them. We also have improved our analytical techniques significantly since 1978.

Mr. **Torricelli**. I am certain you think, though, that thousands of Americans who may have been impacted by dioxin, some carrying them in their bodies—isn't there a reason to believe that your research and conclusions on the impact of dioxin should have preceded rather than followed their introduction into the environment?

Dr. **Gehring**. Could I respond to that? Our research on the impact of dioxin has been longstanding, indeed.

Congressman Torricelli, you were not here, but we recognized, when we first starting producing 2,4,5-T back in 1950, that there was a potential at that time for chloracnigen. Obviously, we do not want to harm our workers in any way, including chloracne, as well as our customers. We did do studies. At that time you could not analyze down at the levels we are talking about now, but we developed a rabbit ear bioassay for the cloracnigenic effect.

Subsequently, there was an explosion—not an explosion, I am sorry—there was a process change in 1964. There was some contamination of dioxin in the work environment, and we did have some chloracne. We immediately went in there and cleaned that up. We again used the rabbit ear bioassay to do this work.

We have conducted lifetime studies on dioxin. We have done reproduction studies, studies on birth defects in animals. We have had a continuing program to ascertain and elucidate the risk of this material.

Mr. TORRICELLI. In fact, the complete impact on the human body is still not known? Isn't that accurate?

Dr. GEHRING. I think that you could say that for just about any material known to man.

Mr. TORRICELLI. Yes, but you have concluded—and I have heard your company conclude previously—that there no evidence at this point of what the impact of dioxin is on the human body. My point is a simple one and a general one, aside from some of the specifics raised here today, and that is that the American people now are concluding that their Government did not protect them from those who would harm the environment. I am wondering the conclusion they can draw about those who produced these materials, whether they are willing to protect them, either. That record seems unclear to me as well.

Dr. GEHRING. As I indicated, we have spent literally millions of dollars, in addition to this Trace Chemistries of Fire, to conduct these studies and evaluate human health effects and, to the best of our judgment, eliminate contamination of our work environment, of our products, and of material going to the environment.

I do feel that a considerable amount of work has, indeed, been done. We have lowered the content, for example, the concentration of the material in 2,4,5-T, and we did this prior to the time it was actually legislated, if you will, or regulated to those levels. We have done a considerable amount. To the best of our capability and ability to do these studies, we have done them.

Mr. TORRICELLI. I spoke with a representative of your company who told me at one point that, while it was true that dioxin had worked itself into the human bodies, into the food chain of some sort, there was no proven impact that it had on human health. If it had no proven impact on human health, therefore, it should not be a significant matter of concern.

Does that characterize the philosophy of your——

Dr. GEHRING. No. There has never been a lack of concern about the effect of this material on human health. We are concerned about the effect of any material on human health. We do these studies to assess what that impact may be, and then to preclude exposures adequate to cause effects on human health. Therefore, there is no lack of concern.

When you consider the fact that here we were—we, Dow—taking samples of the environment, and when we could not find that it was only due to the production of chemicals, looking for other sources of this material—obviously, there is a concern. We published these data to make them available to other concerned people, scientists and Government as well, in the open literature.

Mr. TORRICELLI. Thank you.

Thank you, Mr. Chairman.

Mr. SCHEUER. I thank you for your testimony.

I just want to make two points.

First, we have been sparring a bit on the degree of intervention by Dow into the EPA report, the scientific report, before it was available for peer review. I do not think that Dow has any exclusive responsibility for this. I think much of the blame rests with EPA. In my opinion, it was a sorry, low point in the history of the regulatory process for this interference, this invasion, by censorship, by deletion, for that to have taken place before the scientific report was finished. It does not reflect well on Dow, and it reflects very poorly on EPA. I devoutly hope that it will not happen again under the splendid leadership that EPA is about to acquire.

As to the second point about your concern, your demonstrated concern, for human health and the possible effects of dioxin that you have just given us a moment ago, I have every reason to believe that this subcommittee will request both the Centers for Disease Control and the EPA to make such a study of soil samples, both in Midland and within the Dow facility.

Your demonstrated concern for human health will be put to the test at that time, and you will have an excellent chance to display your bona fides—in effect, to put up or shut up on giving the Nation's top scientists access to those soils and a chance to scrutinize them and examine them for their possible toxicity, to their possible impacts on human health, so that both the Government and your industry, and above all the American people, will be satisfied that, whatever the knowledge is, it will be explored, it will be developed, and it will be made public and proper regulatory actions will follow after that.

Thank you very much for your testimony.

We will now move ahead to the EPA panel: Mr. Val Adamkus, regional director of the Chicago office; Mr. Andersen; Mr. Amendola; Dr. Clark; and Mr. Bremer.

May I ask, who besides Mr. Adamkus will be testifying or answering questions?

Mr. ADAMKUS. Mr. Chairman, it all depends who you are going to ask. Dr. Clark is available.

Mr. SCHEUER. OK. You are all available.

Do any of you object to testifying under oath?

Mr. ADAMKUS. No, sir.

Mr. SCHEUER. OK. Would you please stand?

Do you swear that the testimony you are about to give will be the truth, the whole truth, and nothing but the truth, so help you God?

Mr. ADAMKUS. I do.

Mr. ANDERSEN. I do.

Mr. AMENDOLA. I do.

Dr. CLARK. I do.

Mr. BREMER. I do.

Mr. SCHEUER. All right. You will now be testifying under oath.

Mr. Adamkus, why don't you take the 7 or 8 minutes, as was our practice for the last panel, to give us your testimony, and then I am sure that the panel will have some questions for you.

Your testimony will be reprinted in full in the record following your oral presentation.

Please proceed.

STATEMENT OF VALDAS V. ADAMKUS, ADMINISTRATOR, EPA REGION V, CHICAGO, ILL., ACCOMPANIED BY ROBERT M. ANDERSEN, ASSOCIATE REGIONAL COUNSEL FOR WATER, TOXICS, AND GENERAL ADMINISTRATION; GARY A. AMENDOLA, CHIEF, OHIO FIELD INVESTIGATIONS SECTION; KARL E. BREMER, CHIEF, TOXIC SUBSTANCES SECTION; AND DR. J. MILTON CLARK, HEALTH EFFECTS SPECIALIST, TOXIC SUBSTANCES SECTION

Mr. Adamkus. Thank you very much, Mr. Chairman.

I have a statement I am going to present to you.

During the late 1970's and early 1980's, the Great Lakes States, comprising region V, including the State of Michigan, expressed a growing concern over the amounts of toxicant pollutants which were being discharged into the environment. One of the States' and EPA's foremost concerns was the increased levels of dioxin and furan pollutants, which are highly toxic substances.

On December 2, 1980, the Canadian Government released their findings regarding dioxin contamination in gull eggs taken from the Great Lakes. The findings included data on dioxin contamination of gull eggs found in Saginaw Bay and at other locations in Lake Huron. The Canadian Environmental Minister, John Robert, submitted a report to the State Department and urged the United States to undertake a thorough investigation of dioxin pollution in the international waters which form the common border between the United States and Canada.

As part of region V's ongoing efforts to further understand and control dioxin and furan emissions in the Great Lakes region, I directed the staff of region V to compile relevant information and data on the health and environmental effects of dioxin and furan pollution in the area. A first draft of the report was prepared by Dr. Milton Clark of region V's Office of Toxic Substances in April and May 1981.

That first draft included, among other presentations:

One, an identification of commercial sources of dioxins and furans;

Two, a summary of the toxicological effects of dioxins and furans on animals and humans;

Three, a synopsis of Dow Chemical Co.'s study of the dioxins at its Midland, Mich., facility;

Four, references to other important dioxin studies;

Five, reference to Dow's role in the dioxin problem in Michigan; and

Six, conclusions regarding the sources of dioxins, with recommendations for further study and administrative action.

Note was made in the report of acceptable levels of human consumption of fish flesh taken from the waters in the area.

Dr. Clark's initial report was distributed to other region V staff for review and a copy was also submitted to the headquarters dioxin work group. Since the dioxin work group had been established by EPA headquarters in Washington as experts on this subject, that committee was deemed the logical choice to conduct a review of the report.

Successive drafts of the report were developed throughout the period May 1981 through July 1981 when markups of the drafts, changes, and comments were received from headquarters by region V. A review of the various drafts of the reports, which have been provided to this subcommittee, illuminates the evolution of the work product. At various times during the review process, headquarters officials insisted that headquarters approval for release of the report could not be given without changes being made.

Among the changes insisted upon by EPA headquarters was the deletion of several conclusions and recommendations contained in the report relative to human consumption of contaminated fish, of a synopsis of dioxin and furan health data, and of references to EPA's Alsea, Oreg. dioxin study. These changes were made over the objection of EPA region V staff members involved in the preparation of the report. Much of the deleted information, however, was already public information.

On June 13, a Toronto, Canada, newspaper, which had obtained a copy of an early draft report from an unnamed source, published information from the draft. Sometime after June 18, 1981, region V learned that a copy of a draft report was given to Dow Chemical Co. by Dr. John Hernandez, Deputy Administrator of EPA. Dow provided comments on the report to EPA.

Dow's objections centered around EPA's conclusion that Dow's Midland facility was a major source of dioxin contamination in the Tittabawassee and Saginaw Rivers and Saginaw Bay, Mich. Dow officials also asserted that, contrary to EPA's risk evaluation in 1978, the dioxin contamination at the Midland site itself did not constitute a substantial risk of injury to health or the environment under section 8(e) of the Toxic Substances Control Act.

In the meantime, the premature release of the information by the Toronto newspaper had imparted a degree of urgency to the need for publication of the report. It became evident to region V staff that the report would not be approved for publication by headquarters officials quickly enough to meet the concerns of the State of Michigan, in particular, unless the changes were made.

Although the changes being proposed both by headquarters and by Dow would affect the public impact of the report, they would in no way diminish its usefulness for the region's original primary purpose, which was to compile the relevant existing data in one place for its more effective use and dissemination by the regional staff in their ongoing efforts to develop a control strategy for dioxin emissions in the region. I, therefore, determined that it was in the public interest to publish the report without further delay in its edited form.

EPA region V has been actively seeking information from Dow Chemical Co. concerning all toxicant pollutants generated at its Midland, Mich. facility. A formal information request was issued to Dow on January 20, 1981, pursuant to section 308 of the Clean Water Act.

The information being sought under the Clean Water Act is needed to assist the State of Michigan in the development of effluent limitations for toxicants based upon best available technology for Dow's next NPDES permit, to allow EPA to perform its oversight and review of the permit under the Clean Water Act, and to enable EPA to determine whether Dow has violated any requirements of the act.

Region V made repeated efforts to obtain Dow's compliance with the information request, including an agreement to accept Dow's proposal of a phased release of the information. It became obvious to region V, however, that Dow would not produce the required information, and that continuing negotiations would only serve to further delay efforts to develop a permit.

Therefore, region V submitted a litigation referral to EPA headquarters on April 1, 1982, recommending a civil action against Dow for refusal to comply with the information request. The matter was referred to the Department of Justice by headquarters in Washington on May 6, 1982, and a complaint was filed in the eastern district of Michigan on January 17, 1983.

In September of 1981, region V also initiated a field study of toxicant contamination in Dow's wastewater discharge and in the waters of the Tittabawassee River near the Dow Midland plant. The study included, among other inquiries, an analysis of the accumulation of dioxin in fish placed in cages in the vicinity of Dow's Midland plant. Region V determined that the study was needed at the Midland site for several reasons.

First, Dow's Midland plant is a large, complex, chemical manufacturing facility containing many processes with the potential for discharge of a wide variety of toxic organic pollutants. The discharge of these compounds should be controlled through appropriate limits in an NPDES permit.

Second, previous studies have shown high levels of dioxin in fish downstream of the facility. Additional data was needed to better define the extent to which current discharges from Dow were causing dioxin contamination in fish.

Third, Dow had not adequately responded to information requests made under the authority of the Clean Water Act, making it necessary for the State and EPA to conduct an extensive investigation of the company's pollutant discharges.

As part of the region V's study of toxicants at the site, EPA placed fish in cages at specific locations in the Tittabawassee River:

One, upstream of Dow plant;

Two, in the mixing zone of Dow's effluent in the river; and

Three, downstream of the Dow plant.

The data summary for the caged fish study and the analysis of Dow's effluent should be finalized in a week or two. Preliminary results show that dioxin exists in Dow's effluent and accumulates in fish in the Tittabawassee River. However, some of the analyses have not yet been completed. This portion of the study was designed to determine whether, and to what extent, dioxins and furans are being discharged by Dow to the Tittabawassee River, and what impact the discharge has on fish in the river near the Dow plant.

Among other actions being taken by the State of Michigan and region V relative to the Dow Midland site is the development of licenses and permits controlling the storage, treatment, and disposal of hazardous wastes. Region V will continue to work with the State of Michigan to study the dioxin problem in the Tittabawassee River, to issue an NPDES wastewater discharge permit for Dow's

Midland plant which provides adequate controls for dioxin and other toxic pollutants, and finally to initiate any additional actions deemed necessary and appropriate by EPA staff.

I want to thank the subcommittee for giving me the opportunity to make a statement regarding region V's dioxin efforts. I will be glad to answer any questions which you may have, to the best of my ability and recollection.

With me today are the regional officials who were most closely involved in working on dioxin problems in region V and I am sure they will be able to address any technical or other questions which require elaboration.

Thank you very much.

Mr. SCHEUER. Thank you very much, Mr. Adamkus.

[The prepared statement of Mr. Adamkus follows:]

STATEMENT OF VALDAS V. ADAMKUS, REGIONAL ADMINISTRATOR, U.S. ENVIRONMENTAL PROTECTION AGENCY

Good afternoon, Mr. Chairman and Members of the Subcommittee. I am Valdas V. Adamkus, Regional Administrator of the United States Environmental Protection Agency (EPA), Region V. With me today are Robert M. Andersen, Associate Regional Counsel for Water, Toxics and General Administration; Gary A. Amendola, Chief, Ohio Field Investigations Section; Karl E. Bremer, Chief, Toxic Substances Section; and Dr. J. Milton Clark, Health Effects Specialist for the Toxic Substances Section. We are here at the request of the Subcommittee to answer your questions regarding Region V's efforts to study and control dioxins and furans in the Great Lakes area.

During the late 1970s and early 1980s, the Great Lakes states comprising Region V, including the State of Michigan, expressed a growing concern over the amounts of toxicant pollutants which were being discharged into the environment. One of the states' and EPA's foremost concerns was the increased levels of dioxins and furan pollutants, which are highly toxic substances. On December 2, 1980, the Canadian government released their findings regarding dioxin contamination in gull eggs taken from the Great Lakes. The findings included data on dioxin contamination of gull eggs found in Saginaw Bay and at other locations in Lake Huron. The Canadian Environmental Minister, John Roberts, submitted a report to the State Department and urged the United States to undertake a thorough investigation of dioxin pollution in the international waters which form the common border between the United States and Canada.

As part of Region V's ongoing efforts to further understand and control dioxin and furan emissions in the Great Lakes region, I directed the staff of Region V to compile relevant information and data on the health and environmental effects of dioxin and furan pollution in the area. A first draft of the report was prepared by Dr. Milton Clark of Region V's Office of Toxic Substances in April and May of 1981. That first draft included, among other presentations: [1] an identification of commercial sources of dioxins and furans; [2] a summary of the toxicological effects of dioxins and furans on animals and humans; [3] a synopsis of Dow Chemical Company's Study of dioxins at its Midland, Michigan facility; [4] references to other important dioxin studies; [5] reference to Dow's role in the dioxin problem in Michigan; and [6] conclusions regarding the sources of dioxins, with recommendations for further study and administrative action. Note was made in the report of acceptable levels of human consumption of fish flesh taken from the waters in the area.

Dr. Clark's initial report was distributed to other Region V staff for review and a copy was also submitted to the Headquarters Dioxin Workgroup. Since the Dioxin Workgroup had been established by EPA Headquarters as experts on the subject, that committee was deemed the logical choice to conduct a review of the report.

Successive drafts of the report were developed throughout the period May, 1981 through July, 1981 when markups of the drafts, changes, and comments were received from Headquarters by Region V. A review of the various drafts of the reports, which have been provided to this Subcommittee, illuminates the evolution of the work product. At various times during the review process, Headquarters officials insisted that Headquarters approval for release of the report could not be given without changes being made. Among the changes insisted upon by EPA Headquarters was the deletion of several conclusions and recommendations contained in the report relative to human consumption of contaminated fish, of a synopsis of dioxin and furan health data, and of references to EPA's Alsea, Oregon dioxin study. These changes were made over the objection of EPA Region V staff members involved in the preparation of the report. Much of the deleted information, however, was already public information.

On June 13, a Toronto newspaper, which had obtained a copy of an early draft report from an unnamed source, published information from the draft. Sometime after June 18, 1981, Region V learned that a copy of a draft report was given to Dow Chemical Company by Dr. John Hernandez, Deputy Administrator of EPA. Dow provided comments on the report to EPA. Dow's objections centered around EPA's conclusion that Dow's Midland facility was a major source of dioxin contamination in the Tittabawassee and Saginaw Rivers and Saginaw Bay, Michigan. Dow officials also asserted that, contrary to EPA's risk evaluation in 1978, the dioxin contamination at the Midland site itself did not constitute a substantial risk of injury to health or the environment under Section 8(e) of the Toxic Substances Control Act.

In the meantime, the premature release of the information by the Toronto newspaper had imparted a degree of urgency to the need for publication of the report. It became evident to Region V staff that the report would not be approved for publication by Headquarters officials quickly enough to meet the concerns of the State of Michigan, in particular, unless the changes were made. Although the changes being proposed both by Headquarters and by Dow would affect the public impact of the report, they would in no way diminish its usefulness for the Region's original primary purpose, which was to compile the relevant existing data in one place for its more effective use and dissemination by the regional staff in their ongoing efforts to develop a control strategy for dioxin emissions in the Region. I therefore determined that it was in the public interest to publish the report without further delay, in its edited form.

EPA Region V has been actively seeking information from Dow Chemical Company concerning all toxicant pollutants generated at its Midland, Michigan facility. A formal information request was issued to Dow on January 20, 1981, pursuant to Section 308 of the Clean Water Act. The information being sought under the Clean Water Act is needed to assist the State of Michigan in the development of effluent limitations for toxicants based upon Best Available Technology (BAT) for Dow's next NPDES permit, to allow EPA to perform its oversight and review of the permit under the Clean Water Act, and to enable EPA to determine whether Dow has violated any requirements of the Act. Region V made repeated efforts to obtain Dow's compliance with the information request, including an agreement to accept Dow's proposal of a phased release of the information. It became obvious to Region V, however, that Dow would not produce the required information, and that continuing negotiations would only serve to further delay efforts to develop a permit. Therefore, Region V submitted a litigation referral to EPA Headquarters on April 1, 1982, recommending a civil action against Dow for refusal to comply with the information request. The matter was referred to the Department of Justice by Headquarters on May 6, 1982, and a complaint was filed in the Eastern District of Michigan on January 17, 1983.

In September of 1981, Region V also initiated a field study of toxicant contamination in Dow's wastewater discharge and in the waters of the Tittabawassee River near the Dow Midland Plant. The study included, among other inquiries, an analysis of the accumulation of dioxin in fish placed in cages in the vicinity of Dow's Midland plant. Region V determined that the study was needed at the Midland site for several reasons. First, Dow's Midland plant is a large, complex, chemical manufacturing facility containing many processes with the potential for discharge of a wide variety of toxic organic pollutants. The discharge of these compounds should be controlled through appropriate limits in an NPDES permit. Second, previous studies have show high levels of dioxin in fish downstream of the facility. Additional data was needed to better define the extent to which current discharges from Dow were causing dioxin contamination in fish. Third, Dow had not adequately responded to information requests made under the authority of the Clean Water Act, making it necessary for the state and EPA to conduct an extensive investigation of the company's pollutant discharges.

As part of Region V's study of toxicants at the site, EPA placed fish in cages at specific locations in the Tittabawassee River: [1] upstream of Dow plant; [2] in the mixing zone of Dow's effluent in the River; and [3] downstream of the Dow plant. The data summary for the caged fish study and the analysis of Dow's effluent should be finalized in a week or two. Preliminary results show that dioxin exists in Dow's effluent and accumulates in fish in the Tittabawassee River. However, some of the analyses have not yet been completed. This portion of the study was designed to determine whether, and to what extent, dioxins or furans are being discharged by Dow to the Tittabawassee River, and what impact the discharge has on fish in the River near the Dow plant.

Among other actions being taken by the State of Michigan and Region V relative to the Dow Midland site is the development of licenses and permits controlling the storage, treatment, and disposal of hazardous wastes. Region V will continue to work with the State of Michigan to study the dioxin problem in the Tittabawassee River, to issue an NPDES wastewater discharge permit for Dow's Midland plant which provides adequate controls for dioxin and other toxic pollutants, and finally to initiate any additional actions deemed necessary and appropriate by EPA staff.

I want to thank the Subcommittee for giving me the opportunity to make a statement regarding Region V's dioxin efforts. I will be glad to answer any questions which you may have to the best of my ability and recollection. With me today are the Regional officials who were most closely involved in working on dioxin problems in Region V and I am sure they will be able to address any technical or other questions which require elaboration.

Mr. SCHEUER. Were there any other occasions than the ones you described in which Dr. Hernandez ordered you to change scientific reports in ways that were contrary to the scientific evidence that was in your possession?

Mr. ADAMKUS. Mr. Chairman, Dr. Hernandez never directly ordered me for any changes.

Mr. SCHEUER. How did the changes take place?

Mr. ADAMKUS. Through the conversations between the staffs of region V and headquarters staff, as has been identified in my statement.

Mr. SCHEUER. Weren't you given to understand that on this dioxin report if the changes were not made that Dow Chemical had suggested, that Washington would not give you permission to release the report?

Mr. ADAMKUS. It was specifically expressed to us by the headquarters staff.

Mr. SCHEUER. Were there any other occasions in which that kind of request came to you to make changes that you felt were inconsistent or contradictory to the scientific evidence you had in your possession?

Mr. ADAMKUS. In relation to this report?

Mr. SCHEUER. Or any other report.

Mr. ADAMKUS. Not specifically ordering the changes in any of the reports.

Mr. SCHEUER. All right, let me remind you. In a letter dated September 18, 1981, to Mary Lou Munts of the Wisconsin House of Representatives you stated, and I quote,

> Our view is that detergent phosphate limitations provide valuable protection for the Great Lakes through reducing the loading of phosphorous and helping to control accelerated eutrophication. Whether controls are involved or confirmed is a matter of State and local governments' prerogative.

Now on March 23, 1982, which was just a few months later, you stated to them that,

> Our view is that priority should be given to encouraging State and provincial government efforts to obtain voluntary limits of phosphorous in household detergents and a reasonable and practical measure to control industrial sources of phosphates.

Now in the first letter you talked about detergent phosphate limitations. In the second letter you sort of encouraged voluntary action by State and provincial governments, presumably meaning provinces of Canada.

Isn't there a difference between those two letters?
[The material referred to follows:]

UNITED STATES
ENVIRONMENTAL PROTECTION AGENCY
REGION V
230 SOUTH DEARBORN ST.
CHICAGO, ILLINOIS 60604

SEP 21 1981

SEP 18 1981

Honorable Mary Lou Munts
Wisconsin House of Representatives
125 West State Capitol
Madison, Wisconsin 53702

Dear Ms. Munts:

Thank you for your letter of September 4, 1981, requesting testimony on Assembly Bill 533 concerning detergent phosphate limits. I have enclosed a statement which reflects the facts of the matter based upon the information available in our Offices at this time.

Our view is that detergent phosphate limitations provide valuable protection for the Great Lakes through reducing the loading of phosphorus and helping to control accelerated eutrophication.

Whether controls are involved or confirmed is a matter of State and local governments' prerogative.

If we may be of further assistance, please advise.

Sincerely yours,

Valdas V. Adamkus

Valdas V. Adamkus
Acting Regional Administrator

Enclosures

STATEMENT ON DETERGENT PHOSPHATE BANS WITHIN THE GREAT LAKES BASIN
Presented to Wisconsin Assembly Environmental Resources Committee
Representative Mary Lou Munts, Chairperson

Representative Munts, honorable committee members: Thank you for your invitation to present the information that we have concerning the use of phosphates in laundry detergents in the Great Lakes Basin.

In brief summary we can report the following: (1) The U.S. and Canada have recognized accelerated eutrophication of the Great Lakes as a serious problem and have formalized their concerns and commitments in the U.S./Canada Water Quality Agreements of 1972 and 1978. The central purpose of the Agreements is to restore and maintain the chemical, physical, and biological integrity of the waters of the Great Lakes Basin Ecosystem. (2) Major adverse environmental changes occurred in Lake Michigan and Green Bay due to increasing phosphorus loadings. (3) Detergent phosphate limits have proved to be effective by substantially reducing the amount of phosphorus reaching treatment plants. (4) Reductions in phosphorus loadings have shown positive environmental benefits in both the Great Lakes and inland lakes. Recision of the Wisconsin detergent phosphorus controls are likely to reverse some of these improvements through five contingency inputs due to wastes that escape treatment. (5) It appears that eutrophication problems in Green Bay are of such severity that additional measures such as control of nonpoint sources of phosphorus will be necessary to avoid anoxic conditions. Thus, the reductions in phosphorus loading resulting from detergent phosphate controls are of particular importance in that area. (6) Progress in the development of nonphosphate detergents and their wide use in areas where bans exist have resulted in a variety of commercially available nonphosphate detergents which are safe, provide a broad range of performance from adequate to excellent (when used under appropriate conditions), have generated widespread consumer acceptance, and are available at market costs equivalent to the current costs of high phosphate detergents. (7) There are reports of both indirect consumer costs and taxpayer savings associated with detergent phosphate limits, but there are no difinitive studies available of the relative performance, indirect consumer costs and consumer response to use of various phosphate and nophosphate laundry detergent formulations. Available figures show ranges of values for these costs and savings which heavily overlap. (8) The widespread social acceptance of existing controls indicates that indirect consumer costs are not excessive and/or consumers are willing to make adjustments in their laundering procedures to contribute to improved water quality in their lakes and streams.

I. Introduction

In response to increasing concern among scientists, public officials, and the general public over the deteriorating condition of the Great Lakes, the U.S. and Canada entered the 1972 Water Quality Agreement. Much of the Agreement focused upon the need to control accelerated eutrophication being caused by excessive amounts of phosphorus discharged to the Lakes. Highly visible evidence of accelerated eutrophication was present in heavy growths of algae in western Lake Erie and in harbors, bays and nearshore waters of Lakes Michigan, Huron and Ontario. Algal blooms clouded the waters making them aesthetically unattractive and adding to the cost of treating drinking water. Masses of filamentous algae formed mats which resulted in the closing of beaches. Less obvious but more important than the dramatic nearshore problems, the biota of the open waters was feared to be in irreversible ecological decline. In order to control eutrophication, the Agreements called for a major effort to reduce the discharge of phosphorus to the Lakes. A key portion of the effort included control of detergent phosphates.

The Great Lakes themselves are not only of major importance to the six States in Region V for transportation, recreation, commercial fishing and water supply but also because the drainage basin of the Lakes includes the majority of Region V's population and industry. As a result, much of Region V's pollution control effort is directed toward protecting the environment within the Great Lakes Basin. In addition to the six States of Region V, portions of New York and Pennsylvania are also within the Basin. In order to coordinate Great Lakes efforts among EPA Regions and provide oversight and coordination of state and federal implementation of the U.S./Canada Water Quality Agreement, the Great Lakes National Program Office (GLNPO) has been established and located in Region V with the Regional Administrator serving as National Program Manager for the Great Lakes.

II. General Ecological Perspective

Last year the International Joint Commission's Phosphorus Management Strategies Task Force documented the fact that major environmental changes have already occurred in Lake Michigan - that is, there have been historical increases in total dissolved solids, chloride, sulfate and combined sodium and potassium (See Figure 1)[1] based on in-lake surveys or water intake data.[2] It is likely that increases in these major ions also reflect increases in phosphorus and nitrogen, as well.[3] However, the record for phosphorus is less clear than the major ions since phosphorus is more prone to leave the water column through biological uptake or adsorption to sediment particles which may or may not result in recycling.

Although water chemistry is important in measuring change, it is change in the living populations which provides the clearest indication of ecological disruption. In Lake Michigan, definitive changes have occurred in plankton populations [10,11] including a shift from diatom populations toward the dominance of other species favored by nutrient rich conditions. Cladophora, a green filamentous algae, has become a problem along many sections of the Lake Michigan shoreline.[12] Additionally, a red alga, Bangia, is invading the harbors of Lake Michigan although its increase may be more a result of increasing salinity than of phosphorus enrichment.

After 1977 large decreases were observed in total phosphorus in the southern basin of Lake Michigan, i.e., the trophic status of this Lake has improved considerably.[20] This improvement is due to a combination of factors: construction programs to improve wastewater treatment plants, meteorology, and detergent phosphorus bans.

Although we cannot allocate how much of the improvement is due to the detergent phosphorus bans, scientists are convinced that the bans are responsible for at least part of the improvement because total phosphorus concentrations leveled off at the Chicago water intakes between 1972 and 1973 when the Indiana phosphate detergent ban became effective.[21] Since improvements in municipal and industrial discharges came later than the detergent phosphorus ban, it is quite clear that the Indiana detergent phosphate ban was responsible for some of the improvement in water quality in Lake Michigan at that time.

Many choice, formerly abundant commercial fish species, such as lake trout, blue pike, whitefish, sauger and lake herring have drastically declined or disappeared from their former habitats in the Lakes (See Figure 2).[1] While these declines are the result of multiple factors, there is little question that environmental changes outlined above have affected these stocks.

While it takes careful examination to identify the ecological disruption occurring in the waters of the open lakes, such disruption is often more visible in nearshore areas and embayments. Green Bay is a good example. While at least portions of the Bay appear to have always been relatively enriched with nutrients compared to the open lake, the accelerated decline of water quality in the Bay since mankind's arrival is well established. Historical decreases in dissolved oxygen have been observed[4] as has the resulting change in the nature and abundance of biota.[5] In southern Green Bay, for example, the formerly abundant mayfly, hexagenia, disappeared along with other organisms associated with clean water conditions. Some improvements have occurred, but problems associated with accelerated eutrophication continue as discussed in Section V below.

III. Phosphorus as Related to Great Lakes Eutrophication

By the time that the Great Lakes Water Quality Agreement of 1972 was signed, phosphorus had been identified as the limiting nutrient for all of the Great Lakes and most inland lakes.

The target loadings and remedial measures were developed by a task force of scientists in cooperation with State, Provincial and Federal Governments, as part of the Water Quality Agreement. In the case of Lakes Superior and Michigan, the remedial measures reflect a carefully considered estimate of how much phosphorus can be allowed if control is to be obtained over nuisance algae, assuming that the 1 mg/l requirement is implemented at municipal treatment plants. The limits represent the best scientific opinion at this time as to reasonable measures needed for achieving water quality objectives and provide the basis for developing a phosphorus management strategy in the Great Lakes.

As a follow up to the 1978 Agreement, the Phosphorus Management Strategies Task Force was created to further review phosphorus loadings and remedial measures. Their 1980 report confirms the objectives and, while it recommends against further tightening of treatment requirements at treatment plants, it recommends "that existing laws and regulations to control the phosphorus content of detergents in the Great Lakes Basin be retained and that controls be extended."

IV. Importance of Detergent Phosphate Bans for the Great Lakes

The Task Force found that continuation of existing detergent phosphate bans are essential since they provide a measure of phosphorus control for five contingency inputs to the Lakes as follows:

(1) Communities with discharges greater than 1 MGD and where waste treatment programs are not in compliance with the 1 mg/l effluent phosphorus limits,

(2) communities with combined sewer overflows,

(3) collection systems and treatment plants which malfunction,

(4) communities with discharges of less than 1 MGD without phosphorus removal facilities; and

(5) households which are unsewered.

The Task Force also found that, for wastewater treatment plants required to meet the 1 mg/l limit, the reduced levels of influent phosphorus resulting from detergent phosphate reductions provided definite benefits. The extent of treatment necessary to achieve 1 mg/l is reduced, as is consumption of energy and chemicals, together with the production of sludge with its associated disposal costs.

Several studies have addressed the economic issues of the chemical feed system and sludge handling/disposal. Table 1, Appendix 2, provides an overall comparison of the savings in both the chemical feed system and sludge handling/disposal at municipal wastewater treatment facilities. The table indicates that the expected savings as derived by Folsom and Oliver (1980) is three times less than that given by the Michigan Department of Natural Resources (MDNR) (1981), the Metropolitan Washington Council of Governments (MWCOG, 1981) and the U.S. Environmental Protection Agency, Region V Phosphorus Committee (1977). Expressed on a per household basis (2.8 person/household), the cost range for these operations as given by Folsom and Oliver is \$.81 - \$2.10/household/year, while the range from MDNR, MWCOG and Region V is \$2.38 - \$6.58/household/year. Appendix 2 provides a more detailed discussion of these economic issues.

Phosphorus detergent controls were initiated in the U.S. and Canada in the early to mid 1970's and have been found to be effective. These phosphate bans were effective in reducing wastewater phosphorus concentrations. Decreases of 40-60 percent (from 20.1 mg./l. to 6.3 mg./l.) were achieved by the Metropolitan

Sanitary District of Greater Chicago,[13] in Detroit, Michigan,[14] Monroe County, New York,[15] Erie County, New York,[15] and a large number of municipal wastewater treatment plants in Indiana[16] (See Figure 3 and 4). Voluntary reductions by the detergent industry in areas where legislated controls have not been imposed have reduced the proportion of detergent phosphorus present in municipal wastewater to a range of 30-35 percent of the total influent load [17] (see Table 1, Appendix I). While the increment of phosphorus reduction gained through bans is now reduced due to voluntary partial reductions in detergent phosphates, the high marginal cost of removal through increased treatment adds to the value of further reductions in detergent phosphates.

The level of phosphorus control provided by a detergent phosphate ban for each of the five contingencies identified by the International Joint Commission Task Force varies considerably. The impact of the bans appear greatest at non-compliant sewage treatment plants and communities with combined sewer overflows. We offer the following facts:

1. Impact at Non-compliant Major Treatment Plants: There are 24 such plants on Lakes Superior and Michigan, and four of these are in the State of Wisconsin, (Appleton, Menomonee Falls #2, Portage, Sheboygan).[18] All of the non-compliant plants are located in States with a legislated ban; and they are located on two lakes which, this year will just barely meet their target commitments under the Water Quality Agreements. If the ban in any one of these States (Wisconsin, Minnesota, Michigan or Indiana) were eased, the phosphorus discharge from the non-compliant plants would rapidly increase, and then it is unlikely that the U.S. could meet its commitments.

2. Impact at Communities with Combined Sewer Overflows (CSO): Most cities around Lake Superior and Lake Michigan have combined (sewage and rainwater) sewer discharges. Following heavy rainfall they discharge raw sewage into the Lake or into rivers near the Lake. Using the Ohio EPA estimate that the CSO discharges are equivalent to 10 percent of that contained in the total municipal wastewater flow at all plants prior to wastestream treatment, CSO discharges to the Lakes are obviously a major source of lake pollution.

   For example, the estimated total 1980 major municipal wastewater flow to the Great Lakes Basin from plants discharging over 1 million gallons/day (MGD) in Wisconsin was 365 MGD. Assuming that the no-ban influent total phosphorus concentration was 7.6 mg./l. and the post-ban influent total phosphorus concentration is 4.5 mg./l., and that 10 percent of municipal wastewater flows are discharged prior to treatment at CSOs, then the following estimates can be made:

   No Ban: (365 MGD) x (7.5 mg/l) x (3.785) (10%) = 1036 Kg/day = 378 MT/yr.

   Post Ban: (365 MGD) x (4.5 mg/l) x (3.785)(10%) = 622 Kg/day = 227 Mt/yr.

   (3.785 is a conversion factor for converting gallons to liters)

If the detergent phosphorus ban was withdrawn in Wisconsin, the phosphorus discharge to Lake Michigan and Lake Superior would increase by approximately 151 metric tonnes per year, further jeopardizing our commitment to meet target loads for these Lakes under the Water Quality Agreements.

3. Impacts Related to Great Lakes Loadings from Private Waste Disposal Systems:

Contamination of the Great Lakes from privately owned systems depends upon a large variety of factors including population pressures, local siting requirements, failure rates, age of the systems, quantity of wastewater produced by individuals in a household, concentration of phosphorus pollutant in the septic tank effluent, number of systems in any Great Lakes tributary watershed, and stream and river transport processes. Based on two Canadian pilot watershed studies in the Saugeen and Grand River basin, [19] the contribution of private septic systems to tributary loads in the more populous U.S. may range upwards of several hundreds of metric tons of phosphorus for each of the Great Lakes. Compounding this present load with an additional 33 percent increase in loading [17] from septic tanks due to recision of the statewide phosphate detergent bans could also jeopardize the U.S. commitment under the Water Quality Agreements.

4. Impacts During Treatment System Failures and From Small Communities Without Phosphorus Removal Facilities:

Detergent phosphorus control provides a measure of protection against increased phosphorus loadings that result when sewage treatment plants malfunction or there is a temporary bypass due to overloading of the collection system or the treatment plants. Such occurances may not be frequent at any one location, but must be recognized as part of total loading.

Municipal treatment plants handling wastewater flows less than one million gallons per day are not required to comply with a 1 mg/l total phosphorus effluent concentration. The 1978 U.S.-Canadian Great Lakes Water Quality Agreement excludes these facilities in its directives for controlling phosphorus, as do most State and provincial laws which pertain to municipal waste treatment. If the phosphate detergent controls now in place in Wisconsin were eased, the additive combined inputs from these two sources could also impair the ability of the U.S. to meet our commitments for Lake Michigan under the Water Quality Agreements.

To assist in reducing the phosphorus loads described above, the U.S.-Canada Water Quality Board in 1980 restated its continued commitment to control of phosphorus in household detergents.

V. Special Consideration for Green Bay and Nearshore Areas of Lake Michigan

Beyond the important general considerations of meeting the U.S. target loading commitments for Lakes Superior and Michigan, phosphorus reductions are also needed to solve intensive localized problems such as exist in Green Bay.

As noted in Section II, Green Bay is an example of where localized conditions illustrate the need for nutrient control. In addition to disappearance of Hexagenia and other organisms associated with clean water, even tolerant species such as sludgeworms were reduced in numbers and, in some cases, eliminated entirely. From about 1969 until 1977 the mouth of the Fox River was known as a desert for invertebrates.[6] No doubt, the main cause of the extreme conditions of the rivermouth and extreme southern end of the Bay were the result of biological oxygen demand (BOD) generated from municipal and industrial wastes. However, algal oxygen demand accelerated by phosphorus enrichment would also have been a factor. As control of BOD is achieved, algal demand may well become a more significant factor.

Great strides have been made in reducing BOD loadings from the Fox River where a tenfold reduction has been achieved during the past decade.[7] While this has resulted in improvements in fishery conditions in the River and portions of the Bay closest to the River, problem conditions still exist further out in the Bay. A survey by the GLNPO found severe oxygen depletion in the hypolymnionic waters of the Bay over a 20-square mile area in September of 1980 [21] suggesting that point source BOD reduction will not be sufficient to bring about upgrading of the trophic status of the Bay. The 1980 survey obtained samples one meter above the bottom and found dissolved oxygen levels to be as low as 0.8 mg/l. Dissolved oxygen levels at the actual sediment/water interface were no doubt substantially lower, perhaps reaching total anoxia.

Extreme oxygen depletion not only can have lethal effects upon benthic organisms but can also result in the release and recycling of nutrients and other substances previously held by sediment. Burns[9] suggests that when dissolved oxygen concentrations fall below 0.4 mg/l at one meter from the bottom, anerobic conditions occur at the sediment/water interface resulting in nutrient release.

Although the GLNPO survey found the dissolved oxygen levels to be slightly above the 0.4 mg/l value, it is quite probable that worse conditions existed earlier in the year under other weather conditions. Further work is needed to better understand the Bay as a hydrologic system and establish a nutrient budget. However, its hypolymnionic oxygen depletion appears to be quite similar to the central basin of Lake Erie where a relatively thin hypolymnion becomes anoxic due to sediment oxygen demand caused by the decay of organisms settling out of its eutrophic waters. While the problem may be aggrevated by BOD from tributary sources, it is basically due to eutrophication which, in turn, is due to excessive phosphorus loadings.

It is quite likely that some degree of control over nonpoint sources of phosphorus from land runoff will be necessary to obtain the degree of phosphorus reduction needed to control accelerated eutrophication. Any proposed reduction in controls, such as detergent phosphates limits, would need to be compensated through more stringent controls on other phosphorus inputs to the Bay.

VI. Advantages and Disadvantages of a Detergent Phosphate Ban in Wisconsin:

An extensive review of the detergent phosphate issue was previously prepared by the Region V, U.S. Environmental Protection Agency Phosphorus Committee in June 1977, and we have previously provided a copy of this paper to Representative Munts. This 1977 position paper is a major input to the Water Quality Board's review, and we recommend your careful reading of it. In particular I wish to draw your attention to Table 3-3 on page 33, which summarizes the advantages and disadvantages of a Phosphate Ban in the State of Wisconsin. This Table is included as Table 2 in Appendix 1 of this statement. The environmental benefits, economic benefits and disadvantages are discussed on pages 36-51 of the Region V Position Paper, and we recommend this discussion to you as well.

The EPA committee found advantages of bans to be:

(a) Environmental Benefits: immediate reduction of eutrophication rate of receiving waters, immediate reduction of sludge generated, immediate reduction of total dissolved solids added to receiving waters, and immediate reduction of energy consumption.

(b) Economic benefits: cost savings for chemical and sludge disposal, conservation of phosphorus for food production, conservation of alum and ferric chloride for other industrial uses, reduced need for treatment at small plants by reducing influent phosphorus loadings.

The Region V Committee found the disadvantages of a detergent phosphate ban to be costs which consumers may or may not encounter with use of nonphosphate detergents, depending upon local water supplies. The Committee went on to give an overall evaluation of substantial taxpayer-consumer savings in the State, if a phosphate ban was implemented.

It should be noted that some nonphosphate detergents, formulated with carbonate builders and without a sodium silicate additive, build up deposits in washing machines when used in areas having hard water. It should also be noted that nonphosphate detergents formulated with such anti-corrosion additives such as sodium silicate are readily available in the market place at competitive prices.

We trust that the information provided above is helpful to you.

UNITED STATES
ENVIRONMENTAL PROTECTION AGENCY
REGION V
230 SOUTH DEARBORN ST.
CHICAGO, ILLINOIS 60604

REPLY TO ATTENTION OF
5RA

MAR 23 1982

Assemblywoman Mary Lou Munts
Chairperson
Environmental Resources Committee
State Capitol
Madison, Wisconsin 53702

Dear Ms. Munts:

In previous correspondence I have provided you with technical information concerning the problem of accelerated eutrophication in the Great Lakes Basin caused by excessive amounts of phosphorus entering the lakes from a variety of sources. Since this issue continues to be of interest to you, I would like to share with you some further information on the matter.

As part of the current negotiations between the U.S. and Canada on Annex 3 of the 1978 Agreement relating to phosphorus, the U.S. Environmental Protection Agency (USEPA) has extensively reviewed and analyzed not only current and projected phosphorus loadings, but we have also examined the full range of voluntary and regulatory measures available to meet loading targets and achieve positive environmental results in the most cost effective manner. For the Upper Lakes (Superior, Huron, and Michigan) we expect that proposed load reductions will be accomplished with the achievement of the 1 mg/l phosphorus effluent concentration at municipal waste treatment plants discharging more than one million gallons per day. For Lakes Erie, Ontario and localized problem areas such as Saginaw Bay and Green Bay, further measures to reduce phosphorus loadings would need to be implemented. These further measures could include voluntary: agricultural and urban non-point source control programs; detergent phosphate limitations; and the control of industrial discharges of phosphorus.

The selection of such measures and in what areas would be by the Parties with the cooperation and concurrence of State governments and would not be mandated by federal legislation. In particular, it is USEPA policy that a range of voluntary options exist to further reduce phosphorus loadings to the Great Lakes. It is our view that priority should be given to achievement of the 1 mg/l effluent concentration of phosphorus at municipal plants; to State and Provincial government efforts to obtain voluntary limits of phosphorus in household detergents; and to reasonable and practical measures to control industrial sources of phosphorus.

We fully recognize that the States are the principal jurisdictions in any phosphorus reduction program and we will continue to work closely with them on this and other matters affecting the water quality of the Great Lakes.

Sincerely yours,

Valdas V. Adamkus

Valdas V. Adamkus
Regional Administrator

cc: Assemblyman Randall J. Radtke
Madison, Wisconsin

Mr. **Adamkus**. In spirit there is not, sir. Its approach is different. If you will allow, I can describe——

Mr. **Scheuer**. Please do.

Mr. **Adamkus**. As you probably well know, the original position of EPA, going to the previous administrations, is that EPA was in support of their ban for the phosphates in the detergents. Sometime in late 1981, when the issue came up before a couple of State legislatures in the different States—specifically, the first occasion was the State of Ohio was considering implementation or the ban of phosphates. The word from headquarters came that the policy of this agency is that we are not going to insist on ban, but it should be determined by the State as a voluntary process.

Mr. **Scheuer**. Isn't that a significant change?

Mr. **Adamkus**. It is. It is a major change.

Mr. **Scheuer**. We understand that on March 22, 1982, Dr. John Hernandez met with FMC Corp. officials, and they discussed the administration's policy on phosphates. My question to you is, did Dr. Hernandez order you to change your policy and advocate voluntary limitations on phosphates?

Mr. **Adamkus**. He did not directly order me to change the position. He called me on March 22 very late in the afternoon advising me that——

Mr. **Scheuer**. When you were tired and your defenses were down.

OK. Please proceed.

Mr. **Adamkus**. He advised me that the company's representatives were with him, FMC, and they would be flying to Chicago in the company's plane and asked me to sign the letter on phosphorous to the Wisconsin legislators on our phosphorous position as far as phosphates are concerned in the Great Lakes.

Mr. **Scheuer**. They were flying out to give you a letter to sign?

Mr. **Adamkus**. He never told me that they were bringing the letter with them, but he told me specifically to sign the letter.

Mr. **Scheuer**. What letter?

Mr. **Adamkus**. I don't know. It never probably existed.

Mr. **Scheuer**. Did they bring out a letter for you to sign?

Mr. **Adamkus**. They came into Chicago. They told me that they would be in Chicago 2½ hours; later, at 7 o'clock, I have to meet them. Therefore, I immediately hung up and stopped my staff, which was leaving already from the office. I told them,

> Pull out everything that we have. Let's prepare our own draft which is consistent with the policy of limiting the phosphorous, which is consistent with the international agreement between the United States and Canada, and present a draft at their arrival in Chicago.

In the meantime, the phone rang again, and the representative—the three gentlemen who were in Mr. Hernandez' office—the lawyer for FMC advised me and apologized for the very late hour; that they will arrive in Chicago at 7 o'clock in the evening and I have to sign the letter, as instructed by Mr. Hernandez.

Mr. **Scheuer**. What letter?

Mr. **Adamkus**. That is a good question.

Mr. **Scheuer**. That's why I asked it. [Laughter.]

Mr. **Adamkus**. I never found out, Mr. Chairman. My immediate response was, Look here, you are right there. Why doesn't Mr. Hernandez sign it himself? Why should you fly to Chicago?

He said, "You heard the instructions." Not to waste any time, I said, "OK. Where do we meet?" He said, "At the Hyatt Regency Hotel at 7 o'clock." This was at 4:30 in the afternoon.

I immediately——

Mr. **Scheuer**. And you didn't know what letter you were supposed to sign?

Mr. **Adamkus**. Absolutely. Nobody told me. I was instructed to sign the letter.

Mr. **Scheuer**. They didn't inform you that they were bringing a letter?

Mr. **Adamkus**. No.

Mr. **Scheuer**. Did they suggest where that letter was coming from? Was it going to come from the tooth fairy?

Mr. **Adamkus**. No, sir.

Mr. **Scheuer**. OK. What happened after that?

Mr. **Adamkus**. I immediately stopped—the staff was stopped already. We immediately went to draft our own draft proposal of the letter which should go, like I indicated to you, to the consistency on our phosphate release policies at that time.

At 7 o'clock we went to meet the gentlemen from Washington. Unfortunately, they were late. We stood in the lobby for 3 hours, until 10 o'clock at night. Finally, they arrived, and I immediately pulled out our draft before giving any opportunity, if the letter existed. I don't know if ever it existed.

Mr. **Scheuer**. But you were trying to cut them off at the pass? You were trying to cut Dr. Hernandez off at the pass in case he had a letter that flagrantly conflicted with what you thought was sound, scientific policy on detergents?

Mr. **Adamkus**. I have to admit yes.

Mr. **Scheuer**. OK. Please proceed.

Mr. **Adamkus**. To my pleasant surprise, the company representatives, with very small corrections they indicated, accepted the letter.

Mr. **Scheuer**. They made some corrections on your letter?

Mr. **Adamkus**. Yes. They suggested the corrections.

Mr. **Scheuer**. And you accepted their suggestions?

Mr. **Adamkus**. It was a comma here and there. They insisted on the word "voluntary" very strongly, and that was consistent with the new policy at Washington EPA.

Mr. **Scheuer**. And that was consistent with the conversation you had with Dr. Hernandez?

Mr. **Adamkus**. Previous. Previous. It was late in 1981.

Mr. **Scheuer**. Yes.

Mr. **Adamkus**. I did not see that region V could institute its own policies, so we just accepted the fact that this is the new policy of the agency. We parted at 11 o'clock at night. At 7 o'clock in the morning we came together to the office. We prepared the letter. I signed it and the letter was delivered to the Wisconsin legislators.

Mr. **Scheuer**. Were you happy with that process, Mr. Adamkus? You are a professional of distinction with credibility——

Mr. **Adamkus**. No, sir. Absolutely not.

Mr. Scheuer. Tell me what your reaction was. As an EPA professional in charge of a vast region, with your responsibility to administer scientific policy in the public interest, what was your reaction to that 11 o'clock signing?

Mr. Adamkus. Sir, what kind of a reaction can you have? You feel like you have a gun against your head and you have to do it.

Mr. Scheuer. Well, I guess you have summed it up better than I possibly could.

Thank you, Mr. Adamkus.

The ranking minority member, Ray McGrath?

Mr. McGrath. Thank you very much, Mr. Chairman.

May I bring the subject back to the original intent of the hearing, that being the EPA oversight hearing on dioxin contamination.

Mr. Scheuer. And also the question of political interference in the scientific process. I think we got to the heart of the matter.

Mr. McGrath. May I, if I can, recant approximately the same kinds of questions I gave to the gentleman from Dow Chemical?

In 1981, January 1981, you requested information from Dow Chemical. Am I correct? Approximately 2½ years ago?

Mr. Adamkus. Yes.

Mr. Scheuer. Subsequent to that you went into court in order to retrieve the information that you were asking voluntarily?

Mr. Adamkus. The period extends a little bit——

Mr. McGrath. It was about 1 year——

Mr. Adamkus [continuing]. Over the years.

Mr. McGrath. It took you about 1 year to get from the process of asking for the information to the process of litigating for the information.

Mr. Adamkus. That is correct, sir.

Mr. McGrath. When did you get the information?

Mr. Adamkus. We still don't have this information yet.

Mr. McGrath. In May—you testified between May and July of this past year, I guess, you—first of all, upon what did you base your conclusions if you did not have all of the information?

Mr. Adamkus. Congressman, I believe we have two different issues right here. One report has been initiated originally by us to pool and evaluate available information, and, second, this is follow-up information which we are trying to gather for the NPDES permit which has been in the process by the State of Michigan and us.

Mr. McGrath. On June 13, Dow has testified that they heard through a newspaper source that there was a report being prepared. Had you been in contact with Dow specifically on this particular report prior to that time?

Mr. Adamkus. No, sir.

Mr. McGrath. Did Dow Chemical receive the draft of the report from you?

Mr. Adamkus. No, sir.

Mr. McGrath. Do you know where Dow Chemical received the draft of the report? From whom?

Mr. Adamkus. I was advised by Dr. Hernandez himself that he had ordered to release the report from headquarters directly to Dow, and I was told at that time that I will receive a call from the company and I have to talk to them.

Mr. McGrath. How does that reconcile with the testimony of the previous witnesses that when they called EPA in Washington that they had no knowledge of the report at that time?

Mr. Adamkus. I can't answer that. I understand that they found out about this from the newspaper reports, the Canadian newspapers' reports—Dow Co.——

Mr. McGrath. Who found out about it?

Mr. Adamkus. I believe the company.

Mr. McGrath. We understand that, but the testimony of the company is that when they called Washington, the EPA headquarters, regarding this particular study, that there was very little knowledge of the study, and that they were referred to your office for a copy of the study or to discuss that study.

Mr. Adamkus. I do not believe that this was exactly their testimony, because I have no knowledge of how the report was delivered to them, who asked whom. I understand that they received this report directly from headquarters, not from us, and nobody actually asked us directly to release any report to Dow. We were just advised by Mr. Hernandez that he has released or he will release the report directly to the company.

Mr. McGrath. When was Mr. Hernandez aware of the existence of the draft of this report?

Mr. Adamkus. I don't know, sir.

Mr. McGrath. How would he have gotten the information that there was a report being drafted?

Mr. Adamkus. Probably, I presume in the same way like the company received—we found out in the newspapers that the report has been leaked. Right after June 13, Dr. Hernandez called me personally and made the inquiries about the report asking—almost accusing—for releasing this report to the press.

Mr. McGrath. Let me just take you back a minute. This report did not exist in Dow's mind until June 13.

Mr. Adamkus. I presume so, yes.

Mr. McGrath. From the Dow testimony at this point, their initial call regarding this report was made sometime subsequent to that and before June 18, when they received a copy of the draft.

What I am trying to elicit here is when Dr. Hernandez received the draft in order for them to have it before June 18.

Mr. Adamkus. We don't know, sir. Nobody ever told us this.

Mr. McGrath. How——

Mr. Adamkus. The headquarters people had the draft report already, previously, for their review, peer review, like I indicated in my statement to you. What have they done—when did they approach Dr. Hernandez, when did they give them the report—that is not to our knowledge.

Mr. McGrath. But somebody on your staff would have had to have given Dr. Hernandez the report in order for him to get——

Mr. Adamkus. The dioxin work group, like I stated in my statement on the record—we released that, the peer review, at the headquarters——

Mr. McGrath. At headquarters?

Mr. Adamkus. At headquarters. And that peer review group at headquarters was directly responsible to Dr. Hernandez. When and how they did it, I don't know.

Mr. **McGrath**. OK. What we are saying now is that there were people at headquarters in addition to people at region V who were working on this peer review of this particular scientific data.

Mr. **Adamkus**. Correct.

Mr. **McGrath**. Nobody in region V gave Dr. Hernandez personally any draft of this particular report—but it was readily available to him?

Mr. **Adamkus**. Yes, sir, in headquarters.

I want to make one point here. The region has released only one single copy to the working group in headquarters, and nobody had any additional copies except region V people.

Mr. **McGrath**. How proper—I am not up to speed on how these things proceed, the scientific studies—how proper is it for a draft of a study—how proper is it for that draft to be released before final completion?

Mr. **Adamkus**. Released to whom, sir?

Mr. **McGrath**. To the public or to anybody.

Mr. **Adamkus**. It is absolutely improper to release any draft documents to the public until they are completely finished and carry their final mark of approval of the agency.

Mr. **McGrath**. How significant would you assess the changes that you were ordered to make—or you didn't—no, you were never ordered, I understand by the testimony, but you were suggested to make in order for this report to be released—how significant would you say those changes were from the fourth draft to the final draft?

Mr. **Adamkus**. Here they are, sir. I believe I have the scientists with me here who could actually spell out to you——

Mr. **McGrath**. Who might that be?

Dr. **Clark**. Could you repeat the question for me?

Mr. **McGrath**. How significant are the changes from the fourth draft—first of all, were you satisfied with the fourth draft as being a scientific document that you would have released as a final draft?

Dr. **Clark**. We have previously testified and run through the scenario of changes made between the second draft and the release of the final draft, which was draft No. 7.

At the time, I would say, of draft No. 2 as well as draft No. 4, the document was reasonably polished. It probably still needed to have some more detailed work in it. I was reasonably satisfied with the quality. It had undergone review by regional people as well as members of the Dioxin Workgroup.

Mr. **McGrath**. Subsequent to the June 18 date, obviously you had a phone call with a Dr. Kagel. Is this your handwriting?

Dr. **Clark**. Correct.

Mr. **McGrath**. Are you familiar with this document?

Dr. **Clark**. Yes.

Mr. **McGrath**. I have three pages of handwritten notes; is that correct?

Dr. **Clark**. Correct.

Mr. **McGrath**. I also have an entire page of handwritten notes regarding replacement language, page 12.

Dr. **Clark**. Correct.

Mr. **McGrath**. How significant was this replacement language on page 12 as compared to the draft, the fourth draft?

Dr. **Clark**. The replacement language was put forward—I am going to give you a little longer answer here—was put forward in order to try to balance what were Dow Chemical's objections that the data which they have reported at Midland did not represent a risk under the Toxic Substance Control Act. They wanted to have that particular piece of information included, which contrasted EPA's evaluation, done in 1978 by headquarters staff, that the data did constitute a risk.

Therefore, what we were doing was balancing in this replacement language Dow's position. To say that that is substantially significant, I don't think it was substantially significant. I wrote up the replacement language along with Mr. Kee, and did provide, I think, a fairly balanced approach, including EPA's position and that of Dow Chemical.

Mr. **McGrath**. In other words, this replacement language is satisfactory to you as a scientist?

Dr. **Clark**. I felt here that I had no objections to that replacement language.

Mr. **McGrath**. When was the draft, the final draft, released?

Dr. **Clark**. The final draft was put out on July 16, 1981.

Mr. **McGrath**. July 16, 1981. In other words, you drafted three additional drafts of the report in a month?

Dr. **Clark**. That is correct, based upon conversations we had with the dioxin workgroup members.

Mr. **McGrath**. Did you feel constrained to work that fast under any orders from anybody at headquarters in order to revise—first of all, how significant was the revision from four to seven?

Dr. **Clark**. The reason we were pushing to put comments in that would be satisfactory to headquarters or remove language that would be satisfactory to them, and run through a number of drafts in a very short time period, was to get the document out to the State of Michigan. The Governor of the State had requested to see the data that had been contained in that report and whatever conclusions, and so forth, that might lead to.

Mr. **McGrath**. Did, in fact, this report—or was, in fact, this report—OK'd, signed off, by anybody in headquarters before you released it?

Mr. **Bremer**. I believe I can answer that.

We had conference calls right up to the last minute we released the report. Finally, we got concurrence from Dr. Marilyn Bracken and her staff on the chlorinated dioxin work groups, as to the fact that they would concur on release of the report at that time, provided all those changes were made. Those changes came in until the last day of distribution or until the last day of finalization of the report.

Mr. **McGrath**. Dr. Clark, what was meant by "believe report title should be changed?"

Dr. **Clark**. We went through page by page of the report with Dow officials, and we started with the title. They did not believe the title was appropriate.

Mr. **McGrath**. What does the phrase "agent orange—want these out" refer to?

Dr. **Clark**. I think Dow objected or made a comment relative to agent orange. I cannot quite recall that. I only really recall two specific issues. The first issue was concerning six lines on page 12 of the draft document, and the second issue that I recall was relative to some comments concerning the Alsea, Oreg., study. I did not take a full set of notes.

Mr. **McGrath**. Do you believe that the difference in versions of what the Dow Chemical people, as opposed to what you people, believed is just the difference in opinion between two sets of scientists?

Dr. **Clark**. If I could give you a brief answer, I would say I don't think it is simply a difference of opinion. There are other independent scientific data and comments relative to Dow's position on combustion generating dioxins, and so forth. There is independent research that contrasts Dow's position.

Mr. **McGrath**. One last question. It is your testimony that from the beginning, or at least from the beginning of the production of drafts of the report, that EPA headquarters in Washington was vitally integrated into the drafting process or some section of EPA headquarters in Washington?

Mr. **Adamkus**. Headquarters got involved on May 12. From then on, it was almost daily exchange. They actively participated line by line.

Mr. **McGrath**. That would be one full month before Dow Chemical had ever heard of or requested any information?

Mr. **Adamkus**. Correct, sir.

Mr. **McGrath**. Thank you.

I have one further question.

Why, then, do you believe that independently people at EPA headquarters made this much of your draft? Why do you believe that they significantly changed your draft? If the testimony of Dow and the testimony of yourself—why do you believe that they wanted this draft changed?

Mr. **Adamkus**. Sir, I cannot speculate on this because I do not have any clue one way or another.

Mr. **McGrath**. Thank you.

Mr. **Scheuer**. Congressman Torricelli?

Mr. **Torricelli**. Thank you, Mr. Chairman.

I get the impression from reading your testimony that, if not for the interest of various State governments and the concern of the Canadian Government, in fact, the dioxin problem, if it had been left to the U.S. Government and the EPA, never really would have been brought forward to the point of investigation. Is that accurate? I get that impression from your testimony?

Mr. **Adamkus**. No, sir; probably the urgency at that time was inspired or initiated because of the interest of the Canadians and publicity.

Mr. **Torricelli**. So, in fact, the American people owe a great deal to our Canadian neighbors for doing a job that has finally made the Environmental Protection Agency look at the dioxin problem?

Mr. **Adamkus**. Like I said, the question of urgency at that time—we were involved before.

Mr. **Torricelli**. Let me ask you this, Mr. Adamkus. Did you take an oath of office when you began as regional administrator?

Mr. **Adamkus**. No; it was never conducted.

Mr. **Torricelli**. You never took an oath of office?

Mr. ADAMKUS. No.

Mr. TORRICELLI. That is good, because let me suggest to you the following, and that is I think it would be hard to believe at this point, given what you knew about the impact dioxin could have on the American people, the evidence from Midland, where 111 children had birth defects, the possible carcinogenic nature of dioxin; it is hard to believe that you really did your best efforts to protect the American people, isn't it?

Mr. ADAMKUS. I don't believe I have any answer to that, sir. You have to talk to the scientists who actually were involved from the very beginning and it continues——

Mr. TORRICELLI. No, I would like your answer, because let me tell you what I suggest to you, sir. You commented before that you had no choice; you had a gun to your head when changes in this report relating to Dow Chemical were made.

Mr. ADAMKUS. Sir, you are wrong——

Mr. TORRICELLI. The fact of the matter is you had a very real choice—you could have stayed true to your conscience and not followed the directives of Mr. Hernandez. Isn't that accurate?

Mr. ADAMKUS. No, sir, because you are mixing two facts. Those two reports have absolutely nothing to do with it. This is one report from one issue, and this was the just procedures on the second case.

Mr. TORRICELLI. When it was suggested to you that these changes should be made and Dow Chemical made their suggestions to your colleagues, in fact, you did not at any time think you were putting the people in jeopardy by not stating the truth as you knew it?

Mr. ADAMKUS. Yes, I did say the truth from the very beginning, and my colleagues here know that I was resisting all the way through to any changes, and instructions were to my scientists, "Talk to them. Find out the facts. Argue with them until you are blue in the face."

Mr. TORRICELLI. Yes, you resisted, but to the people who as a consequence are going—during that time period that has intervened—to live with the impacts of dioxin, that is not a terrible amount of consolation to them, is it?

Mr. ADAMKUS. Yes, sir. You are wrong, because the report was initiated by me, insisted by me, instructed to the regional people to originate the report, and that report was leaked to the press. I was ahead of the events.

Mr. TORRICELLI. Would you have ever come forward if it had not come to the attention of the American people and the press that these changes had been done and that Dow Chemical had requested some changes? If the truth had not come out to the American people, would you, because of your responsibility as a Government official, have ever come forward voluntarily?

Mr. ADAMKUS. I did, because this information was available and I was pushing my stuff to compile this for me so that I can actively design the program and put something active in the work. If it were not for me, we would not be talking about this report here.

Mr. TORRICELLI. Let me ask you this, and I ask you this generally about the Environmental Protection Agency: I think we were all relieved because of Mr. Ruckleshaus coming to EPA.

Mr. ADAMKUS. I was delighted.

Mr. TORRICELLI. At least I am relieved. I think the American people should be. He has a fine reputation, as the chairman said.

However, we also know that Ann Burford did not run an agency all by herself. Shouldn't those of us who believe that the Environmental Protection Agency should be based on a bipartisan commitment to environmental protection and that these have been serious violations of the public trust—shouldn't we expect those who are part of the policymaking and part of what I believe comes to as close to criminal activity as one can come expect others to resign as well?

Mr. ADAMKUS. Maybe, because I don't consider myself part of this. I was the only one who came out, forward, and resisted that in the way I knew it.

Mr. TORRICELLI. Let me ask this to you and your colleagues: Did you at any point, when hearing the reactions and the comments of Dow Chemical, have the natural human and legal reaction, "Who cares what Dow Chemical thinks?"

Mr. ADAMKUS. Would you repeat this, please?

Mr. TORRICELLI. My question is: I believe if I had been in your position and I had heard what the interests of Dow Chemical were at any point during this, or their changes or suggestions or objections, my reaction would have been, "Who cares?"

Mr. ADAMKUS. We did. We fought for 2 months, line by line, the headquarters people, even with the Dow people, in suggesting to them that they were not accepting those changes. When I was told this document was not going to see the daylight, we did our best to delete insufficient parts of it and keep and insist on what was really significant.

Mr. TORRICELLI. The point I guess we are left with here, sir, is somebody still has to answer to those who are going to suffer from continued or greater contamination of dioxin in the interim. Someone here is going to have to say those people, "Why?" I guess you know it is not going to be enough to tell them that you were told so by Mr. Hernandez. That is not going to be of a lot of consolation.

Mr. ADAMKUS. Sir, I do not know how to convey this to you, but I believe I made it clear that we are continuously, aside of all the difficulties we had in the region—we initiated the studies. We have one study which the architect of it sits to my right. Even despite all the resistance and unaccessibility to allow us to get to the source, we have conducted and we are coming out with the results.

I believe if we are talking today and you and I are exchanging our opinions about this, about dioxin, this is because we persisted and I believe we succeeded.

Mr. MCGRATH. Would the gentleman yield?

Mr. TORRICELLI. Yes.

Mr. MCGRATH. Could this report have been made public without EPA headquarters signing off on it?

Mr. ADAMKUS. No.

Mr. TORRICELLI. Part of what troubles me here, sir, is I think some people lost sight of something, and that is in the flow of command here we have it a little bit wrong. I suppose Mr. Hernandez thought this was what Mrs. Burford wanted. I suppose that Mrs. Burford thought that this is what the President wanted. The fact of the matter is none of you work for any of those people. Who you really work for is the American people. What people seem to stop to think here is that Dow Chemical was not calling the shots. You are really there to protect a lot of people from getting hurt. The fact is a lot of people have gotten hurt. You know, sitting there today, some people are going to get very hurt.

We have seen birth defects. We can suspect cancer. You know some people are going to die, and no one was there to protect them, all because you were concerned about Mr. Hernandez, Mr. Hernandez was concerned about Mrs. Burford, and Mrs. Burford was concerned with Ronald Reagan.

Mr. ADAMKUS. I don't have a comment, sir, because you don't listen to us, what we are telling you all the time. That is all that I can say.

Mr. ANDERSEN. I would like to respond.

Mr. TORRICELLI. Go ahead.

Mr. ANDERSEN. Region V has continued in its efforts to study and analyze the problem. One of the most important aspects of that problem is the discharge into the Tittabawassee River. For a period of approximately 1 to 1½ years, we negotiated with Dow to attempt to get the information necessary to develop that permit. It is a matter of fact that the State of Michigan is the primary agent in developing that permit.

However, we offered our technical and legal assistance to them, which includes use of our legal staff and our technical staff, to develop a BAT permit. We went to Dow, tried to negotiate that with them. When it became obvious that it was impossible to get the information—the chairman questioned them, and they have assured us they will let us on the site now if we have protocols. I wish the chairman would have asked them that a year ago, about the 308 request, because we are now in court simply because region V will not quit, will not stop pursuing the information that is necessary. We will assist the State in developing the NPDES permit.

In addition to that, almost simultaneously, we embarked on a caged fish study, which Mr. Amendola and the scientists can speak to. That is an integral part, even though Dow at the same time refused to let us put fish in its effluent on its property and refused to let us sample fish from its sewage lagoon. We moved in the direction that we thought was the greatest concern, and that is in the river. We moved as expeditiously as possible, completely unrelated to the data gathering.

I think the Congressmen should recognize that the purpose of that study was to gather existing information. That information, for the most part, existed in the literature already. The enforcement efforts and the efforts that our water division undertook were something independent from that and are proceeding.

Mr. TORRICELLI. What finally is your expectation now of where we go from here with Dow Chemical.

Mr. ANDERSEN. There are a number of things that have to be pursued. The 308, the first question, we litigated this issue already, by the way, in the Illinois district court, where the region, with very little assistance from headquarters or the Department of Justice, litigated the issue and won it on December 28. We have the authority under 308 of the Clean Water Act to go up the pipe to obtain information in internal waste streams, to obtain information about processes. That is on appeal in the seventh circuit.

I think that will have a tremendous impact on the Dow litigation, which is more or less the same question.

Another thing that has to be addressed is the land deposition of dioxin on the site. To date, all that we have, in spite of continuing requests under the Resource Conservation and Recovery Act, is Dow's own samples. They could not tell you today where those five samples were placed, but I think I can tell you that they are wrong at least in telling you that all five of them were on the site. I believe two of them, at least that is what the scientific people tell me, are around the site.

We do not have enough information. As Mr. Adamkus has stated elsewhere, the dioxin work group just in the region is right now working on further responses to the problem, both on the land and with respect to their discharge.

Mr. **Scheuer**. Would my colleague yield?

Mr. **Torricelli**. Certainly, Mr. Chairman.

Mr. **Scheuer**. Mr. Andersen, as you have no doubt noticed, we are very much concerned about the testing of the soil samples and whether that was adequate to protect the public interest, and you have no doubt gleaned from the conversation that took place before that we have every intention of requesting EPA region V and the Centers for Disease Control together to design a protocol and go in and do an absolutely professional, painstakingly thorough sampling within the county and within the confines of the Dow plant to determine whether the concentrations of dioxin have reached critical levels that imply critical health effects to the citizens of Midland County and to the employees of Dow Chemical.

We have had reports, and these are not scientifically valid, that of a sample of 40 women, 40 pregnant women who are married to Dow engineers, chemists, and professionals, that 90 percent of them had serious birth defects in their infants or suffered miscarriages. We intend to ask you to investigate that, as well as the soil samples.

In view of your own skepticism that you have expressed about the five soil samples that Dow evaluated and analyzed, how would you react to a formal request by this subcommittee, and perhaps the Health Subcommittee of the Commerce Committee, to go in there and do a job and find out what the truth is, turn over every stone that needs to be turned, and tell the American people and the Congress what your estimate is as to the level of dioxin that is there and whether this constitutes a health threat to the American people, the residents of Midland County, and the employees and their spouses of Dow Chemical?

Mr. **Andersen**. It would be absolutely positive, and, with all due respect, Mr. Chairman, I must say that the gentleman to my right is ahead of you and we are working on that as of this day, as a matter of fact.

There are any number of tools that are available to the agency, all of which can be stopped at the gate of the plant, and they are all legal problems, which is my bailiwick. Those tools are being analyzed right now for those same purposes. Therefore, I would say region V's goals and plan, at least in a generic form, coincide with what you have just said.

Mr. SCHEUER. Do you wish——

Mr. ADAMKUS. Absolutely, Mr. Chairman.

Mr. SCHEUER. We have had a statement from Dow Chemical that they are concerned with the possible health impacts on humans of dioxin concentrations and that, assuming the protocol is professionally designed, that they will cooperate with that.

I yield back to my colleague.

Mr. TORRICELLI. Thank you, Mr. Chairman.

I know that Mr. Adamkus does not think that I listened very well, so I want to assure him that I am going to be listening very well for the next 2 years. I am certain, sir, that we are going to be seeing each other again and often. I hope that this time when there comes an opportunity to prepare the kind of indictment of a corporation that that document was in its original form of Dow Chemical we do not go to the felon and ask him to rewrite his indictment.

I also hope something else. I do not know the State laws in some of the areas that you administer, but I know in my State of New Jersey any corporate official with the kind of knowledge that it appears to me that these gentlemen had who tried to restrict investigations of the EPA, conducted themselves in this manner, would not have a civil problem at; they would be going to jail. I think that is useful because it is time in this country we started to not think of polluters anymore as people who just upset the environment, but as the kind of criminals that they can be.

Anyway, we shall meet again.

Mr. ADAMKUS. Thank you very much.

Mr. TORRICELLI. Thank you.

Mr. ADAMKUS. Congressman, I would like to just go on the record. I responded to you because I felt hurt. I was beaten up all the time by my superiors, and I was beaten now by you.

Mr. TORRICELLI. Yes. Well, my only point was: Remember who you work for. They can beat you all they want, but if you do not—this is an old problem in public service in who you work for and when you stand up and say, "Enough!" You had an opportunity to say, "Enough!" I hope next time you do not miss it.

Thank you.

Mr. SCHEUER. Congressman Chandler.

Mr. MCGRATH. Would the gentleman yield for just 1 minute?

Mr. CHANDLER. Yes. Thank you, Mr. Chairman. I yield to my colleague.

Mr. MCGRATH. Just to set the record straight, the EPA in region V and any other region that I know of is an advisory, scientific organization; am I correct? You are not regulatory in your charge from the Government; am I correct?

In other words, you have no power to go in and close down a facility that you suspect as being a polluter or dangerous to the health and safety? You turn that information over to the State regulatory agency; am I correct?

Mr. ANDERSEN. Mr. McGrath, if I may answer that question, if it gets to the point where we believe that injunctive relief is necessary in a court, the process is rather burdensome, although in January—if I can use an example to explain the process, I will—in

January we learned in East Cape Gerardo that there was a company, an energy company, that was operating a storage tank facility and also was disposing of PCB's on the site. The storage tanks were contaminated with PCB's.

The ordinary process if for us to develop, with our scientists, a litigation referral which goes to headquarters, and headquarters then refers it to Justice, and the action is taken. However, the roles that will be played by the lawyers and the scientists, as you must be aware, vary.

In a case such as that, the region is very active, start to finish. We referred the case on the 7th of January, and we had a final judgment on the 17th of January. In other cases that are more complicated and more complex, it may well be that the Justice attorney in Washington will take the lead in the case; it may well be that the assistant U.S. attorney in the area where we file the case will take the lead, but it varies from case to case.

The short answer to you is on an injunctive relief situation where health is a problem, we initiate it, we refer it to headquarters, where their independent group of scientists and lawyers will review it, and then it is referred to Justice for filing.

Mr. **Chandler**. I would like to follow up on that line of questioning because I think that my colleague from New York is hitting on something here that is really important, and that is, what is the significance of the document that was obviously influenced by employees of the Dow Chemical Co?

Mr. Andersen, you were answering the question of EPA region V's role. The State of Michigan, which if it is like the State I represent, Washington, has clean water laws of some kind on its books—is that correct?

Mr. **Andersen**. That is correct. All States do. In our particular region, sir, almost all the environmental laws that we have federally have been delegated to the State as the primary actors.

Mr. **Chandler**. What is an NPDES study? What is its use and significance? What do you do with that?

Mr. **Andersen**. In the Clean Water Act there are controls that have to be devised for different forms of effluent from industrial and municipal discharges. That comes in the form of the National Pollutant Discharge Elimination System [NPDES] permit. That permit in our region is developed by the State, and it has controls for any number of substances.

With respect to the permit that Dow has, there are existing controls on total dissolved solids, dissolved oxygen, total suspended solids, biological oxygen demands, chlorides, PH-dissolved solids, and oil and grease at the final discharge point.

You note that what that lacked was a lot of toxic substances. Those effluent guidelines are in the process even now of being developed. For many toxic chemicals, they simply do not exist.

Therefore, in order to control it, the agency has to know about the processes that discharge the chemicals and develop what is known under the Clean Water Act as the best professional judgment, best available technology permit, which is based on technological control at the site. That is different from other effluent-based or water quality-based permits that are the standard type of permits that would be available.

Mr. **Chandler**. Would the report that is in question here be used by the State of Michigan in the permit process or in the enforcement of its laws for regulation of water?

Mr. **Andersen**. If you are talking about the initial report that Dr. Clark developed——

Mr. **Chandler**. Yes.

Mr. **Andersen**. That was not the purpose of the report.

Mr. **Chandler**. What was the purpose of the report?

Mr. **Andersen**. The purpose of the report, I think as Mr. Adamkus stated, the primary purpose, if I can repeat his testimony, was to compile the relevant existing data in one place for its most effective use in dissemination in the ongoing efforts that develop the control strategy for dioxin emission.

Now as to a permit, the type of information that we would require is very specific. It is not information about dioxin that is in the river. It is information about the toxic chemicals that are in Dow's internal waste streams on their property and the processes that discharge those particular chemicals. That was not information that ever existed in the report that Dr. Clark had begun to develop.

Mr. **Chandler**. What I am trying to get at is sort of the so what of all of this. If that report had—well, let me ask you another question.

I believe it was you who talked about Dow litigation?

Mr. **Andersen**. That is correct.

Mr. **Chandler**. What is the Dow litigation? What is at stake there?

Mr. **Andersen**. The Dow litigation is a chase that region V, after negotiating with Dow for a period of to 1½ to obtain all of the information that I have just referred to, the internal waste stream data and the process-related data, after being unsuccessful in obtaining that by making formal requests, region V in April of 1982 felt that it had no choice but to refer that matter to EPA headquarters for litigation, where we go to the court and ask for declaratory judgment, saying EPA has the right under section 308 of the Clean Water Act to obtain this information that is internal, on the property, and the process information.

Now Dow's greatest concern in that regard, as they have stated here today, is that the process information at least—they are claiming there is a proprietary interest, that it contains information which, if released, would give their competitors an advantage. We do not believe that that is correct, and we have filed a case I believe just 1 month ago, 1½ months ago. Dow has not as of this time answered.

Mr. **Chandler**. Is the question of who is the primary contributor to contamination of the Tittabawassee and Saginaw Rivers—is that a question that is of importance in that litigation?

Mr. **Andersen**. Absolutely. The whole purpose of the litigation is to control dioxin before it gets into the river.

Mr. **Chandler**. If I can stop you there because I want this answer to be very clear, when you, EPA, the headquarters—I do not want to get into the Torricelli misunderstanding here—when EPA asked for and got the change from "EPA concludes" to "EPA speculates" then that is important to the outcome of this litigation that you are discussing?

Mr. ANDERSEN. As a lawyer, no—I——

Mr. CHANDLER. Oh, I misunderstood you. I thought you just said that——

Mr. ANDERSEN. No. As a lawyer, the information that is in that report does not have any impact on the litigation.

Mr. CHANDLER. But I asked——

Mr. ANDERSEN. That was information that had been released before. That conclusion preceded 1979, I believe. That would not have an impact on the litigation which was really seeking information which was different from the information that we already have.

Mr. CHANDLER. All right. I will not beat it to death. I thought you said—and this is from Buzzelli's testimony. He said that Dow has been—the statement was made that Dow has been the primary contributor to contamination of these two rivers. My question was, with regard to this litigation, does that make any difference and how you couch that. The terms "concludes" and "speculates" are very different ones. What I was driving at was, does that make any difference to the outcome of this litigation. Your answer is apparently no, it does not.

Mr. ANDERSEN. No. The outcome of this litigation, Congressman, will be whether or not EPA has the authority under section 308, as a matter of law, to go up the stream, get internal waste stream data, and to get process-related information.

Mr. CHANDLER. If you don't, we ought to change the law so that you do.

Mr. ANDERSEN. The law is very clear to me, and it was very clear to the District Court of Illinois when we litigated it this fall.

Mr. CHANDLER. I have just one final question for Mr. Adamkus.

You talked about, on page 4, the deletion of several conclusions and recommendations contained in the report relative to human consumption of contaminated fish, a synopsis of dioxin and furan health data, and references to EPA's Alsea—that is how you pronounce it; I used to fish in it—Oreg., dioxin study.

What is the significance of those items? What were the conclusions and recommendations that you had in the report that were deleted? What is the significance of those, also this health data, and the references to the EPA's Alsea, Oreg., dioxin study?

Mr. ADAMKUS. The significance of Alsea, as told by my staff, was a great one. I believe that they can repeat to you the scientific basis, how they arrived at this.

I believe at that point I was more or less relieved, knowing that this information already was a public document released in 1978. If that would be the hangup of approval or disapproval of the report at that time, it was not impacting our work or the information. It is not suspended from the general public. It was a public record. It was a matter, probably, of principle that it was not allowed to be included in that particular work, but I would refer for the significance from the scientific point of view—I would like to defer this to Mr. Bremer.

Mr. CHANDLER. All right.

Mr. **Bremer**. The reference on the Alsea study, as we testified to last week, on Friday, during the Dingell committee, was that those studies—the reference to the study remained in the report, the actual reference to it. However, the words "Alsea study" and the other three lines included with that were removed from the report at the request of Dr. Bracken. That was on the last day when we were trying to get the report finalized.

The reference remains in the report. However, the words "Alsea study" and the other lines accompanying that, which I could quote to you probably, if needed, were removed from the report.

Mr. **Chandler**. Mr. Chairman, thank you very much. I have no further questions.

Mr. **Scheuer**. Thank you.

Let me take the opportunity of clearing the air a little bit.

I wish to express my admiration to the Chicago office as a group—to you, Mr. Adamkus, as the chief administrator there, and for your scientific and legal aides, who have expressed themselves so well this afternoon. I want to express my admiration for the way you stood up, for the intrepidity with which you stood up far beyond the call of duty, in resisting the relentless and unremitting pressure from Washington to change your report and to change the regulatory policy as to dioxin, as to phosphates, in ways that you felt were inconsistent with the public interest. To me, it was a remarkable display of devotion to the public interest in the most courageous way that you gave to the American people.

The fact that under our form of government in Washington they make the final decisions is in no way a reflection on the good fight that you made to serve the public interest in a way that you felt was consistent with the scientific data that was available and the way the public interest should be served.

I hope that in the future the decisions will be made by people like you, dedicated professionals, administrators and dedicated professional scientists, and that the corporate polluters, through their proxies at high levels of the EPA Washington officialdom, will not have their way and will not thwart people such as you in making the decisions that you feel are in the public interest.

I feel that you resisted to the last ounce of strength these politically-dictated changes in your science report, changes in your regulatory policy. You finally acquiesced, as you had to, at this 11 o'clock hotel conference when you described that you were under the gun. Those words summed up the whole pattern, this continuous pattern, of misconduct and political interference with scientific objectivity, both in research and in administration.

I hope that this classic example of misconduct and political interference is an era which will end. I hope we have seen the last of that kind of thing.

I congratulate you for your conduct in the field and also for your cooperation with this committee in coming and telling us the truth as you see it, letting it all hang out, so that the Congress in its wisdom and the new Administrator in his wisdom can take the actions that are necessary to prevent this kind of egregious misconduct from happening again, to protect the public interest.

I thank you all very much for your fine testimony.

Mr. **Adamkus**. Thank you very much.

Mr. SCHEUER. We will now go to the last group, which will be professionals from the Centers for Disease Control in Atlanta, the CDC.

We will be hearing from Dr. Houk, Mr. Edmonds, and Mr. Poole.

Do any of you have any objection to be sworn in?

Dr. HOUK. No, sir.

Mr. SCHEUER. OK. Would you please stand?

Do you hereby swear to tell the truth, the whole truth, and nothing but the truth, so help you God?

Dr. HOUK. I do.

Mr. EDMONDS. I do.

Mr. POOLE. I do.

Mr. SCHEUER. All right, you now will be testifying under oath.

Mr. Poole, we will start off with you.

Let me say to all of you that your testimony will be printed in its entirely in the record following your oral presentations. We would ask you to address the 7 or 8 minutes that we have given the other witnesses, hitting the highlights and summarizing your testimony. Then I am sure we will have some questions for you.

Mr. Poole, please proceed.

STATEMENT OF CHARLES POOLE, DOCTORAL STUDENT IN EPIDEMIOLOGY, HARVARD SCHOOL OF PUBLIC HEALTH

Mr. POOLE. Good afternoon.

My name is Charles Poole. I am presently a doctoral student in epidemiology at the Harvard School of Public Health.

As I understand it, this subcommittee is interested in the history of a proposal for an epidemiologic study of birth defects in Midland County, which I began to develop as an employee of the Environmental Protection Agency in 1979.

My testimony today describes the development of that proposal up to the present time. I also briefly describe the history of my relationship with EPA.

After receiving a master of public health degree at the University of North Carolina in 1976, I came to work in Washington for the White House Council on Environmental Quality. In February 1978, I joined the staff of the EPA Office of Toxic Substances.

On September 1, 1981, I left active duty as part of the EPA long-term training program and entered the doctoral program in epidemiology at Harvard. There were two parts to my agreement with EPA.

The first part was my agreement with the EPA training center to repay 3 years of active service for 1 year of support. The second part was an informal agreement with all of my supervisors that I would be granted an additional 9 months of leave without pay to enable me to complete the Harvard residency requirement for doctoral students.

To make a long story short, my application for leave without pay was denied without explanation, but I have no indication that that denial had anything to do with the proposal for the study. I will not go into the details on the decisions that led to my departure, but I would be pleased to answer any questions you might have about it.

My interest in birth defects in Midland County began in March 1979, shortly after EPA had announced an emergency suspension of some of the registered uses of the herbicides 2,4,5-T and silvex. Part of the rationale for the suspension was a study sponsored by the EPA Office of Pesticide Programs of hospitalized spontaneous abortions in an area of Oregon where 2,4,5-T was used on timberline. This is the Alsea study which you have been discussing.

The authors of that study believed they had discovered a seasonal pattern in the occurrence of spontaneous abortions in the exposed area consistent with an increase 1 to 2 months following the spring spraying season.

In response to the EPA study, scientists from the Dow Chemical Co. had submitted Midland County hospital data to show that seasonal patterns like the one reported in Oregon can occur in areas where there are no commercial forests to be sprayed in the spring.

I was asked by the EPA Office of General Counsel, which I will call OGC, to assess the suitability of Midland County as a control area for the Oregon study area. In the course of my evaluation I ran across the data that I would like to show in this figure, if I can. I believe there is a projector available.

These data were produced by the Midland Department of Public Health in 1976 for the National Institute of Occupational Safety and Health study of counties with vinyl chloride production facilities. The data, which come from information recorded on birth certificates, show a sharp increase in Midland County's recorded birth defect rate during the years 1971 through 1974.

During that 4-year period the county's rate was about 2.5 times the rate in the entire State of Michigan during the same period of time or the rate in Midland County itself during previous and subsequent years.

The statistical analyses I performed indicated a low likelihood that the increase was due solely to chance. Approximately 70, or 60 percent of the 113 congenital anomalies recorded on Midland County birth certificates during the 4-year period, exceeded expectation.

One set of possible explanations for this kind of increase consists of factors that influence the diagnosis of birth defects and the recording of diagnoses on birth certificates. Birth certificates frequently provide underestimates of the actual occurrence of birth defects. Larry Edmonds from the Center for Disease Control is an expert on these matters, and part of his testimony will be given today.

I consulted him very early in my inquiries of this situation. My general understanding is that some of the reasons that a birth defect might not be reported on a birth certificate include a judgment by the person filling out the certificate that the defect is too minor to mention or a delay in noticing the anomaly until after the certificate has been completed.

It is possible that the apparent increase in the period 1971–74 could have been due to temporarily increased diagnostic awareness or improved diligence in filling out the birth certificates in Midland County. If so, the excess would represent the birth defects which were occurring at a normal rate but which were merely being diagnosed or reported more frequently than usual. This explanation, in fact, was the one put forth as an opinion by the Michigan Department of Public Health in 1976.

The apparent increase, as shown in the next frame, was not restricted to a single type of birth defect. This fact alone tends in general to support increased diagnosis for reporting as an explanation, as does the fact that two of the categories—genital-urinary and cardiorespiratory defects—include anomalies which are often classified as minor.

On the other hand, reports of clefts of the lip and palate were also elevated. These malformations are never considered minor and might, therefore, be less prone to be transient changes in diagnostic awareness or the completeness of reporting.

I developed a draft proposal in the summer of 1979 for an epidemiologic study to evaluate the apparent increase more thoroughly and systematically. It is that document that I believe has come to the subcommittee's attention.

Mr. Edmonds and I traveled to Lansing, Mich., in July or August 1979 and discussed the proposed project with George Van Amberg and Kennety R. Wilcox, Jr., of the MDPH. We left the meeting with the understanding that the study was worth pursuing and that the MDPH would not only agree to the study, but would conduct a part of it having to do with location of parental residence.

In November 1979 I received an encouraging letter from Mr. Van Amberg.

During the interim, however, I had obtained a clipping from the Midland Daily News from May 1976 in which Dr. H. C. Schwarnweber, Dow Chemical's medical director, described a study the company was planning at the time. The article stated that the study's purpose was in part to address the question of the apparent 1971-74 increase. The Dow Chemical investigation, conducted in 1977, consisted of interviews with wives of Dow Chemical workers with potential for exposure to polychlorinated dibenzodioxins, which I will call PCDD, by virtue of working in the production of 2,4,5-T, pentachlorophenol, and their chemical precursors.

Some 40 percent of the employed adults in Midland County work in the chemical industry, most of them presumably at the Dow Chemical facility.

The PCDD study, which covered a long period of time, including the years 1971-74, offered a good opportunity to see if the apparent increase in these years would also be present in data derived from a source much different from birth certificates: the responses of women to questions posed by interviewers. Such information would not be subject to the same kinds of bias, especially those having to do with the recording of defects, as suspected for birth certificate information. The advent of the Dow Chemical study was the principal reason for my decision to hold in abeyance the plans for the study I was developing.

When I left for Harvard in August 1981, I remained an EPA employee. The OGC asked me to take along and analyze a computer printout of the underlying data from the Dow Chemical study. The study had been completed but not yet published. A magnetic tape of the data, which would have made analysis much easier, was not available.

The OGC said, however, that if I found anything in the data of sufficient interest to a hearing that was ongoing with respect to 2,4,5-T at the agency, a tape could be requested from Dow Chemical. I also had access to a prepublication version of the Dow Chemical report of the study. From it, I knew that, in at least their first published analyses, the Dow Chemical investigators were not planning to address specific time periods such as 1971-74. The paper was published in virtually the same form as I saw it in May 1982.

Beginning in the fall of 1981, while at school, I manually extracted from the computer printout a set of data which formed a case-control study. The case-control study is a major research design in epidemiology. In essence, it contrasts the experiences and characteristics of a group of people who have a disease with those of a comparable group, the controls, who are free of the disease.

One important advantage of case-control studies is that they require data on only a sample of the nondiseased portion of a population, rather than the entire population. This attribute enabled me to perform meaningful analyses without access to the complete Dow Chemical data set in computer-readable form.

I reported my results periodically by telephone to the Office of General Counsel, and in September 1982, as part of a new draft proposal for the countywide study I had been contemplating.

I believe that a scientist who analyzes another scientist's data has an ethical imperative to notify the original researcher of the results before publishing or making other official use of the analysis. In this situation——

Mr. SCHEUER. Mr. Poole, in deference to the time, you have somewhat overrun your time, could you begin to wind it up?

Mr. POOLE. Sure. I would just like to point out what I found in the Dow Chemical data.

In my analysis of the Dow Chemical data, the association between birth defects and PCDD or dioxin was very weak and statistically unstable. That was essentially the finding that the authors of the report had found.

After controlling for important extraneous factors, I obtained an estimate of 1.4 for the rate of birth defects in the exposed group divided by the rate in the unexposed group.

For the years in which the sons and daughters of Dow Chemical employees were born, however, I found a much stronger association. That is in the next frame. There I found essentially the same result that had been apparent in the birth certificate data, a ratio of 2.4 for infants born during the years 1971-74 in comparison to those born in other years.

When I controlled for extraneous factors, that estimate became reduced to 1.9 with a 90 percent confidence interval of 1 to 3.6, which roughly accounts for the role of chance.

In summary, my analysis of the Dow Chemical data supports the rationale for conducting a countywide study to discover the reason or reasons for the so far unexplained increase in recorded birth defects in Midland County during the year 1974. Of course, an important first step would be to analyze the entire Dow data set, and I have given my proposal to Dow and the subcommittee, and of course EPA has it. I am ready to help anyone in any constructive way that I can.

[The prepared statement of Mr. Poole follows:]

Statement of

Charles Poole

Before the

United States House of Representatives

Science and Technology Committee

Subcommittee on Natural Resources, Agricultural Research, and Environment

March 23, 1983

Good afternoon. My name is Charles Poole. I am presently a doctoral student in epidemiology at the Harvard School of Public Health. My curriculum vitae appears at the end of my testimony. As I understand it, the Subcommittee is interested in the history of a proposal for an epidemiologic study of birth defects in Midland County, Michigan, which I began to develop as an employee of the Environmental Protection Agency in 1979. My testimony today describes the development of that proposal up to the present time. I also describe the history of my relationship with EPA.

History of my relationship with EPA

After receiving the Master of Public Health degree at the University of North Carolina in 1976, I came to work in Washington, DC for the White House Council on Environmental Quality. In February, 1978, I joined the staff of the EPA Office of Toxic Substances. My position was staff epidemiologist.

On September 1, 1981, I left active duty as part of the EPA Long-Term

Training Program and entered the doctoral program in epidemiology at Harvard. There were two parts to my agreement with EPA. The first part was my agreement with the EPA Training Center to repay three years of active service for one year of support in the form of salary, tuition, moving expenses, books, and supplies. The second part was an informal agreement with all of my supervisors, through the Assistant Administrator, that I would be granted an additional nine months of leave without pay to enable me to complete the Harvard residency requirement for doctoral students of two academic years. This period includes required course work, written and oral qualifying examinations, and preparations for the thesis project. The plan my supervisors and I had worked out was that, upon my return, I would begin a program of epidemiologic research and that the first project under this program would serve as my thesis experience. My hope was for the Midland County birth defects study to become this initial project.

While preparing for my academic program in the summer of 1981, I sought advice from the EPA Training Officer, Joseph Sullivan, and from Don Nantkes, an EPA employee particularly well versed in personnel matters. They both advised me that my arrangement with my program office, unlike my legal agreement with the Training Center, was completely informal and subject to change at any time. Mr. Sullivan informed me that, in the event I became unable or unwilling to return to EPA, it would be possible for me to serve my obligation at another Federal facility or to reimburse EPA for the non-salary support I had received while on training leave. It was always my intention to return to EPA. Until August, 1982, I believed that my supervisors in the Office of Pesticides and Toxic Substances were still willing to grant me the additional leave without pay that would enable me to complete the non-thesis requirements for my degree.

In August, 1982, my application for leave without pay was approved by my Branch Chief and Division Director, but was denied without explanation by the Office Director, Don Clay. This development took me completely by surprise and had the effect of forcing me to choose between my degree, which I consider essential for my career to progress within the field of epidemiology, and my job. Through the kind and diligent efforts of my Branch Chief, Janet Springer, I was granted a period of leave without pay through the first semester of the 1982-83 academic year. I used that time in unsuccessful attempts to find a way to return to EPA in January, 1983, or to obtain another Federal position. Effective January 24, 1983, I decided to separate voluntarily from EPA. I am now in the process of completing the paperwork for my departure, including reimbursement to the Agency for my training support.

Between August, 1982, and January, 1983, Mr. Clay issued a memorandum stating a policy decision he had made with respect to applications for training leave by employees of the Office of Toxic Substances. I do not know the details of that memorandum, because I was not forwarded a copy. My understanding is that it restricted the number of employees whose applications would be approved for leave for educational purposes to one per year. The memorandum, of course, did not apply to me because the decision about my request had already been made. Nevertheless, the two decisions appeared to be entirely consistent with each other. I have no indication that my work on the proposal for studying birth defects in Midland County had anything whatsoever to do with the decision that led to my departure from the Agency.

I harbor no personal grudge against the Office of Toxic Substances or EPA in general for the conditions and events precipitating my separation. I have been able to readjust my plans satisfactorily. Since September, 1982, I have received support from a National Institute of Environmental Health

Sciences National Research Service Award, administered by Professor Richard Monson of the Department of Epidemiology, and from part-time employment.

History of the Midland County proposal

My interest in birth defects in Midland County began in March, 1979, shortly after EPA had announced an emergency suspension of some of the registered uses of the herbicides 2,4,5-T and silvex. Part of the rationale for the suspension was a study sponsored by the EPA Office of Pesticide Programs of hospitalized spontaneous abortions in an area of Oregon where 2,4,5-T was used on timber land. The authors of that study believed that they had discovered a seasonal pattern in the occurrence of spontaneous abortions in the "exposed" area consistent with an increase one to two months after the spring spraying season. In response to the EPA study, scientists from the Dow Chemical Company had submitted Midland County hospital data to show that seasonal patterns like the one reported in Oregon can occur in areas where there are no commercial forests to be sprayed in the spring. I was asked by the EPA Office of General Counsel (OGC) to assess the suitability of Midland County as a "control" area for the Oregon study area.

In the course of my evaluation, I ran across the data in the Figure, which were produced by the Michigan Department of Public Health in 1976 for a National Institute of Occupational Safety and Health study of counties with vinyl chloride production facilities. The data, which come from information recorded on birth certificates, show a sharp increase in Midland County's recorded birth defect rate during the years 1971 through 1974. During the four-year period, the County's rate was about two and one-half times the rate in the entire State of Michigan during the same period of time or the rate in Midland County itself during previous and subsequent years. Statistical analyses I performed indicated a low likelihood that the increase was due solely to chance. Approximately 70, or 60%, of the 113 congenital anomalies recorded on Midland County birth certificates during the four-year period exceeded expectation.

One set of possible explanations for this kind of increase consists of factors that influence the diagnosis of birth defects and the recording of diagnoses on birth certificates. Birth certificates frequently provide underestimates of the actual occurrence of birth defects. Larry Edmonds from the Centers for Disease Control, whom I understand also has been asked to testify today, is an expert on these matters. I consulted him very early in my inquiry into this situation. My general understanding is that some of the reasons that a birth defect might not be recorded on a birth certificate include a judgment by the person filling out the certificate that the defect is too minor to mention or a delay in noticing the anomaly until after the certificate has been completed. It is possible that the apparent increase in the period 1971-74 could have been due to temporarily increased diagnostic awareness or improved diligence in filling out birth certificates in Midland County. If so, the "excess" would represent birth defects which were occurring at a normal rate but which were merely being diagnosed or reported more frequently than usual. This explanation, in fact, was the one put forth as an opinion by the Michigan Department of Public Health (MDPH) in 1976 (Exhibit 1).

The apparent increase, as shown in Table 1, was not restricted to a single type of birth defect. This fact tends to support increased diagnosis or reporting as an explanation, as does the fact that two of the categories, genito-urinary and cardio-respiratory defects, include anomalies which are often classified as minor. On the other hand, reports of clefts of the lip and palate were also elevated. These malformations are never considered minor and might therefore be less prone to transient changes in diagnostic awareness or the completeness of reporting.

I developed a draft proposal in the summer of 1979 for an epidemiologic study to evaluate the apparent increase more thoroughly and systematically. It is that document that I believe has come to the Subcommittee's attention. Mr. Edmonds and I travelled to Lansing, Michigan in July or August of 1979 and discussed the proposed project with George Van Amberg and Kenneth R. Wilcox, Jr. of the MDPH. We left the meeting with the understanding that the study was worth pursuing and that the MDPH would not only agree to the study but would conduct a part of it having to do with location of parental residence. In November, 1979, I received an encouraging letter from Mr. Van Amberg (Exhibit 2).

During the interim, however, I had obtained a clipping from the Midland Daily News from May, 1976, in which Dr. H.C. Scharnweber, Dow Chemical's Medical Director, described a study the company was planning at the time. The article stated that the study's purpose was in part to address the question of the apparent 1971-74 increase (Exhibit 3). The Dow Chemical investigation, conducted in 1977, consisted of interviews with wives of Dow Chemical workers with potential for exposure to polychlorinated dibenzodioxins (PCDD) by virtue of working in the production of 2,4,5-T, pentachlorophenol, and their chemical precursors. Some 40% of the employed adults in Midland County work in the chemical industry, most of them presumably at the Dow Chemical facility. The PCDD study, which covered a long period of time including the years 1971-74, offered a good opportunity to see if the apparent increase in these years would also be present in data derived from a source much different from birth certificates: the responses of women to questions posed by interviewers. Such information would not be subject to the same kinds of bias, especially those having to do with the recording of defects, as suspected for birth certificate information. The advent of the Dow Chemical study was the principal reason for my decision to hold in abeyance the plans for the study I was developing.

When I left for Harvard in August, 1981, I remained an EPA employee. The OGC asked me to take along and analyze a computer printout of the underlying data from the Dow Chemical study. The study had been completed but not yet published. A magnetic tape of the data, which would have made analysis much easier, was not available. The OGC said, however, that if I found anything in the data of sufficient interest to the hearing, a tape could be requested from Dow Chemical. I also had access to a prepublication version of the Dow Chemical report of the study. From it, I knew that, in at least their first published analyses, the Dow Chemical investigators were not planning to address specific time periods such as 1971-74. The paper was published in virtually the same form in May, 1982 (Exhibit 4).

Beginning in the fall of 1981, I manually "extracted" from the computer printout a set of data which formed a case-control study. The case-control study is a major research design in epidemiology. In essence, it contrasts the experiences and characteristics of a group of people who have a disease with those of a comparable group (the "controls") who are free of the disease. One important advantage of case-control studies is that they require data on only a sample of the non-diseased portion of a population, rather than the entire population. This attribute enabled me to perform meaningful analyses without access to the complete Dow Chemical data set in computer-readable form. I reported my results periodically by telephone to the Office of General Counsel and, in September, 1982, as part of a new draft proposal for the countywide study I had been contemplating (Exhibit 5).

I believe that a scientist who analyzes another scientist's data has an ethical imperative to notify the original researcher of the results before publishing or making other official use of the analysis. In this situation, however, legal questions intervened. While I was still an EPA employee, I requested permission from the OGC to communicate my findings, in the form of my September, 1982 draft proposal, to the Dow Chemical epidemiologists whose data I had evaluated. The OGC did not grant this request, as a matter of strategy in the administrative hearing. I was confident, however, that upon my return to active duty at EPA the OGC would consent to such a communication so that plans for the study could proceed. In just a few weeks, it became clear that I would be leaving the Agency when my leave without pay expired on January 24, 1983. At that point, my status as a former employee with respect to the Dow Chemical data and the judicially imposed protective order under which they had been placed was unclear. The OGC was in the process of deciding upon the most appropriate advice to give me concerning my ability to discuss the data when the Subcommittee announced its plans to invite me to testify. The question then became irrelevant, as I had no intention of withholding this information from Congress and the OGC had no intention of suggesting that I do so. Subsequently, my first step was to write to Ms. Jean C. Townsend, the senior author of the published paper on the Dow Chemical study. I explained my analysis, included my proposal, and indicated the Subcommittee's interest in the matter (Exhibit 6). I also wrote to Mr. Van Amberg at the MDPH (Exhibit 7) and forwarded copies of both letters to EPA, CDC, and the Subcommittee staff.

In my analysis of the Dow Chemical data, the association between PCDD and birth defects was weak and statistically unstable. After controlling for important extraneous factors, I obtained an estimate of 1.4 for the ratio of the prevalence of defects among "exposed" infants to the prevalence among "unexposed" infants. ~~(Table 2).~~ A 90% confidence interval I constructed for this estimate to evaluate the role of chance ranged from 0.8 to 2.2. (A ratio of 1.0 indicates no effect by the exposure and ratios less than 1.0 indicate protective effects.) Thus, although my study of the data does not exonerate PCDD as a possible influence on birth defects, it cannot be taken as strong evidence in favor of such an association.

For the year in which the sons and daughters of the Dow Chemical workers were born, however, I found a stronger association. The estimate of ~~rate~~ ratio was 2.4 for infants born during the years 1971-74 in comparison to those born in other years (Table 2). This estimate is virtually identical to the one that was apparent in the birth certificate data for Midland County as a whole. Moreover, the association was just as strong in the study's comparison group, which contained the children of workers without recorded potential direct PCDD exposure, as it was in the study's "exposed" group. After control for the most important extraneous factors, the estimate became reduced to 1.9, with a 90% confidence interval of 1.0 to 3.6.

My analysis of the Dow Chemical data supports the rationale for conducting a countywide study to discover the reason or reasons for the so far unexplained increase in recorded birth defects in Midland County during the years 1971-74. An important first step would be to conduct a computer-assisted analysis of the entire Dow Chemical data set. I understand that the CDC and the MDPH may have recently initiated data collection or analysis activities which may shed additional light on the subject. I have offered my proposal (Exhibit 5) to all concerned and have reiterated my willingness to contribute in any constructive way I can.

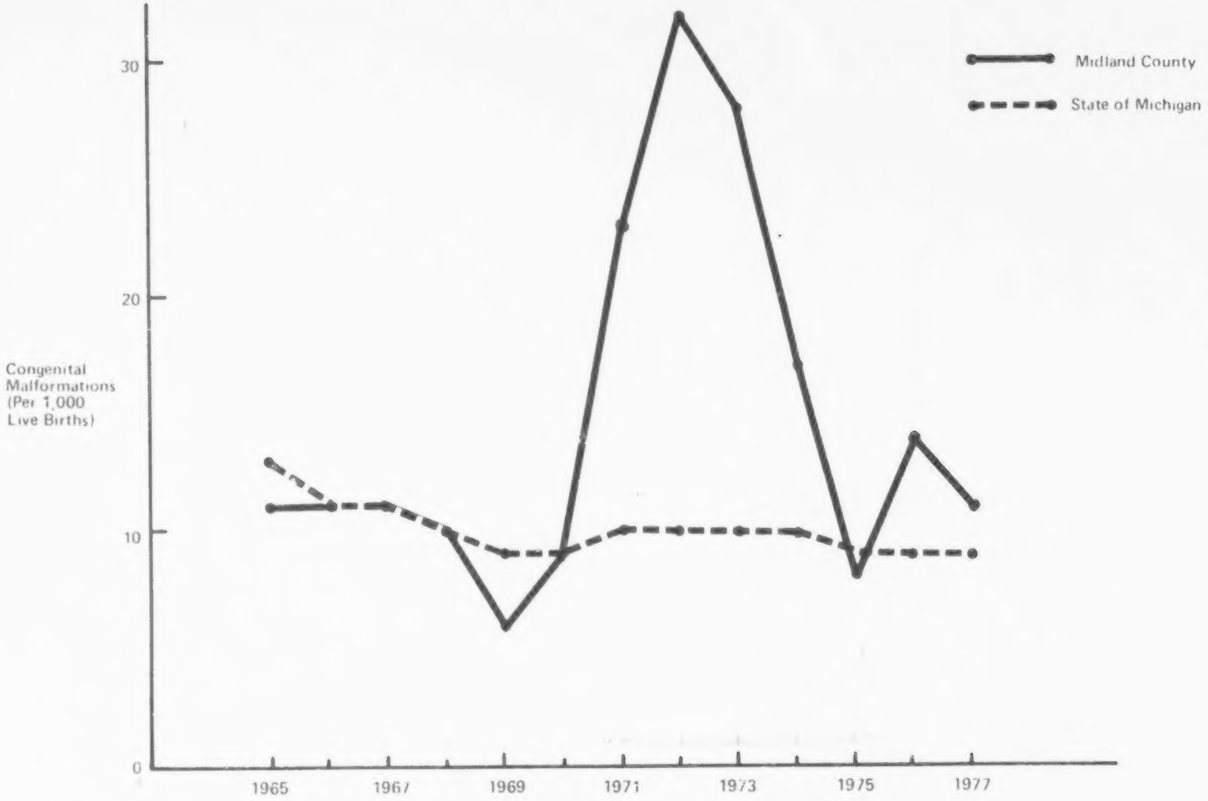
A list of some important factors I believe should be addressed appears as Table 3. The extensive public attention focused on PCDD in the past few days will make any future Midland County study that depends on interviews or questionnaires vulnerable to severe methodologic criticism. Fortunately, objective records can be used to make some evaluation of each of the items in Table 3.

I will be happy to answer any questions you may have.

LIST OF EXHIBITS

1. Letter dated April 30, 1976, from R.G. Rice to Todd Mason.
   Letter dated July 7, 1976, from David B. Johns to Gerald Rice.
   Letter dated July 22, 1976, from R.G. Rice to David B. Johns.
2. Letter dated November 21, 1979, from George Van Amberg to Charles Poole.
3. Article from the Midland Daily News, May 28, 1976.
4. Townsend JC et al. Survey of reproductive events of wives of employees exposed to chlorinated dioxins. Am J Epidemiol 115:695-713, 1982.
5. Poole C. Proposal for a case-control study of birth defects in Midland County, Michigan, 1971-1974. Draft dated September, 1982.
6. Letter dated March 18, 1983, from Charles Poole to Jean C. Townsend.
7. Letter dated March 18, 1983, from Charles Poole to George Van Amberg.

TOTAL CONGENITAL MALFORMATION RATIOS IN STATE OF MICHIGAN AND MIDLAND COUNTY, 1965 – 1977



Source: Data supplied by Michigan Department of Public Health to Dow Chemical Company, 1976.

TABLE 1

CATEGORIES OF BIRTH DEFECTS IN MIDLAND COUNTY, 1971-74

CATEGORY	RATE RATIO*	90% CONFIDENCE INTERVAL
Genito-urinary defects	5.7	4.4 - 7.4
Cardio-respiratory defects	3.1	2.0 - 4.9
Cleft lip and palate	2.8	1.8 - 4.3

* Midland County's rate divided by the rate in the entire State of Michigan.

Source: Michigan Department of Public Health.

TABLE 2

ASSOCIATIONS WITH BIRTH DEFECTS IN MIDLAND COUNTY BIRTH CERTIFICATES AND DATA FROM A STUDY BY TOWNSEND ET AL.

COMPARISON	RATE RATIO	90% CONFIDENCE INTERVAL
Midland County birth certificates		
1971-74 v. other years	2.6	2.1 - 3.2
1971-74 v. State of Michigan	2.5	2.1 - 2.9
Townsend data, 1971-74 v. other years		
Crude estimate	2.4	1.3 - 4.5
Controlled for PCDD, "other medications"*	1.9	1.0 - 3.6

* Extraneous factors for which control was not necessary were: maternal age, smoking, alcohol consumption, x-ray, and use of anti-nausea medications during pregnancy.

TABLE 3

FACTORS TO CONSIDER IN EVALUATING THE APPARENT EXCESS OF BIRTH DEFECTS IN MIDLAND COUNTY, 1971-74

Diagnosis by attending physicians

Recording of defects on birth certificates

Parental residence - city limits (e.g., water supply)
- chemical facility

Parental occupation - chemical industry
- other

Maternal use of medications during pregnancy

Infectious disease

Mr. SCHEUER. Thank you very much. Dr. Houk.

STATEMENT OF DR. VERNON N. HOUK, DIRECTOR, CENTER FOR ENVIRONMENTAL HEALTH, CENTERS FOR DISEASE CONTROL, PUBLIC HEALTH SERVICE, DEPARTMENT OF HEALTH AND HUMAN SERVICES

Dr. HOUK. Thank you, Mr. Chairman.

I am Dr. Vernon N. Houk, the Director of the Center for Environmental Health, Centers for Disease Control, Public Health Service. I am accompanied by Mr. Larry Edmonds, an epidemiologist on my staff.

I am pleased to represent the Public Health Service this morning to discuss CDC's birth defect surveillance activity and our involvement in the birth defect question in Midland, Mich.

CDC maintains two birth defect surveillance systems with a staff of about eight persons. The Metropolitan Atlanta congenital defects program began in October 1967 and is the more complete system because of the multiple intensive methods used to identify infants with birth defects. These intensive methods include review of hospital records, records of local cytogenetic laboratories, and genetic counseling clinics, and of live birth, infant death, and stillbirth certificates. Since its inception in 1967, this surveillance system, encompassing the Metropolitan Atlanta counties, with approximately 25,000 births annually, has registered some 15,000 infants with birth defects.

The birth defects monitoring program, heretofore referred to as BDMP, initiated in late 1974, is a surveillance system collecting data on diagnoses of birth defects in newborns from hospital discharge summaries from approximately 1,200 U.S. hospitals with obstetric services located in 750 counties in 45 States. This system contains data on 150 birth defect categories and includes approximately 1 million births per year. These 150 birth defect categories include individual malformations and grouped malformations covering the entire range of organ systems. Among these 150 are 37 categories we have selected as most helpful in identifying and analyzing national trends in major birth defects.

Data from the BDMP system are generally available for analysis within 6 months after the birth of the infant. Although this system is less complete than the MACDP, it is substantially more complete for those areas for which data are gathered than reporting of birth defects by birth certificate only. In some areas, the only——

Mr. SCHEUER. Excuse me. Could you just clarify something? What is MACDP?

Dr. HOUK. MACDP is the Metropolitan Atlanta birth defect program. That is the first one, the Metropolitan Atlanta congenital defects program, which has 15,000 infants registered since 1968, out of about 250,000 births.

Mr. SCHEUER. Thank you.

Dr. HOUK. With the initiation of the BDMP in 1974, we purchased existing data for 1970–73. These data are used as baseline rates to compare the rates observed on new data acquired each succeeding year since 1974. These periodic reviews look for statistically significant increased rates in each defect category by county and other larger geographic areas. Analysis is performed as often as four times a year on this large volume of data. A statistically significant increase may occur by chance alone, and this fact needs to be underscored. For example, in the phrase "statistically significant at the 0.05 level," we mean that an event could have occurred by chance as many as 5 times out of 100. Therefore, the data must be interpreted cautiously.

CDC first learned of a possible increase in the incidence of birth defects in Midland, Mich., when Mr. Todd Mason, a reporter for a Midland newspaper called Dr. J. William Flynt, at CDC, on March 29, 1976. Mr. Mason said he had data from birth certificates showing that the total malformation rates for Michigan were 9 per 1,000 in contrast to 21 per 1,000 for Midland. Mr. Mason was concerned that these increases were due to vinylchloride production in the Midland area.

After discussing the problems of reporting variation and that the small numbers of birth defects could yield misleading results in interpreting birth certificate data, Dr. Flynt suggested that the next step would be to review the specific diagnoses of the birth certificates.

Mr. Mason called on May 20, 1976, to say that the State health department had investigated the matter further and found that much of the increased incidence was due to better reporting of minor defects. However, for 1970 to 1974 the cleft lip and cleft palate rate was 26 per 10,000, about three times the State rate.

Dr. Flynt pointed out that the rate was similar to and not significantly different from the rate of about 20 per 1,000 found in the very extensive surveillance in the Atlanta area. Mr. Mason first expressed concern at this time that the birth defect incidence might be related to 2,4,5-Trichlorophenoxyacetic acid or 2,4,5-T from which dioxin emanates, as we will discuss later, a herbicide that was produced in the Midland area.

In 1977 we were contacted by Ms. Jean Townsend, epidemiologist, Michigan Division, Medical Department, Dow Chemical Co., who was planning a study of reproductive outcomes of Dow in Midland. In 1976 she was supplied with birth defects monitoring program data for Michigan and for the United States. In May 1978, at her request, we supplied a list of severe birth defects. We further offered to objectively code defects into major and minor types without knowledge of the exposure status of the parents. We were not asked to do the coding.

In the fall of 1978, during our periodic review of the BDMP data, we noted the increased rate of combined cleft lip and palate in the early 1970's for Midland County. In our judgment at the time of this analysis, there was nothing particularly unusual about the increase observed in Midland. The annual incidence of several categories of birth defects by county varied significantly during these same years. It is important to remember that if one looks for increases for each of the 150 birth defects each year in a county, some increases will be observed due to chance alone.

In the spring of 1979, Mr. Charles Poole, epidemiologist, epidemiology branch, office of toxic substances, Environmental Protection Agency, contacted Mr. Edmonds about Mr. Poole's desire to do a study of birth defects in Midland County. He was concerned about the possible association of birth defects and 2,4,5-T production at the Midland plant.

CDC provided Mr. Poole suggestions about the proposed study design and encouraged him to work with the State of Michigan Department of Health. After several discussions with the concerned parties, Mr. Edmonds, Mr. Poole, and officials of the Michigan Department of Health met on November 19, 1979, to discuss Mr. Poole's protocol.

At the November 19 meeting, the study design that was discussed would have included, among other variables, the relationship between residence of the parents of children born with birth defects and proximity to the Dow plant. Similarly, parental occupational exposures would have to be studied.

It was agreed that the study had to consider exposure to all chemicals and not just to the single chemical 2,4,5-T and thus a revised protocol was needed.

We consulted with EPA on the design of the study and encouraged EPA and the State of Michigan to work closely together because the issue of birth defects had been raised several times in the past. We understood that a revised protocol would be forthcoming. Because we were serving as consultants and not as principal investigators, we took no action other than to encourage the principals to investigate this matter.

In 1981, CDC used BDMP data to do state-by-state and county-by-county analysis of 37 selected birth defects for live births from 1970–80. These 37 defect codes were selected by CDC from the larger list of some 150 codes because we felt that they were the most appropriate codes to screen for increases in birth defects related to environmental, mutagenic, and genetic factors.

In September 1981 the preliminary analysis was completed. We sent to each State health officer data for the United States as a whole. The data showed the annual frequency and rate of each defect. The letter offered State and county data if requested by the health officer.

At the request of the Michigan Department of Health, these data for all Michigan counties including Midland were given to Dr. Kenneth Wilcox, State epidemiologist, Michigan Department of Health, in April 1982. For these 11 years combined and 37 selected defect codes, there was only one significant increase for Midland County—dislocation of the hip, a condition with considerable interphysician variance in diagnosis.

Mr. SCHEUER. Excuse me. Does that phrase "interphysician variance in diagnosis" mean that doctors sometimes disagree?

Dr. HOUK. Doctors disagree, and one will call it a dislocated hip, minor or major or not call it at all.

Mr. SCHEUER. Thank you.

Dr. HOUK. Being a physician, I could not say that.

These 37 selected defects included a category for cleft palate alone and a category for cleft lip with or without cleft palate. This distinction was used, rather than all orofacial clefts combined, because in our opinion these two types of defects differ with respect to certain epidemiologic and genetic variables that suggest different etiologic mechanisms.

If, however, the cleft palate alone and cleft lip with or without cleft palate are combined, the previously noted statistically significant increase for Midland County for the early 1970's is found.

Table 1, included as part of this testimony, shows a total by year for 1970–80 of the numbers and the rates of the two defects alone and combined. You can see that for 1971, 1972, 1974, and 1975 there is between a 50 percent and 100 percent increase in combined orofacial defects when compared with the overall Michigan State rate. There is an unexplained increase between 1971 and 1975 in Midland County. The rates since 1975 have returned to expected levels.

The previously mentioned Townsend study of Dow Midland workers has now been published and raises additional questions about orofacial clefts. When one reviews the published report, though not discussed in the text, table 3 of that report shows 10 infants with orofacial cleft defects among 2,422 live births to wives of employees, 1939–75.

This is twice what one would expect and again a twofold increase in the rate of these two defects combined.

In summary, for most categories of the 37 birth defects we found no increases for Midland for the combined years of 1970–81.

The analysis of the 150 categories does show that during these 12 years the total reported combined official defects are elevated about 50 percent when compared to all of Michigan. This elevation occurs predominately because of increases in 1971, 1972, 1974, and 1975. In our opinion these birth defects' codes should be considered separately and not combined because of the causal mechanism where the birth defects may be different.

We do not know the cause of the above increase in the frequency of the combined orofacial clefts during the years or even if there is a specific cause. It may never be possible to find a cause, if any. We remain available, however, to provide assistance to the State of Michigan and others as appropriate.

Mr. Chairman, I know that the 37 codes and the 150 codes and stuff can be confusing and I have listed those out if you choose to put those in the record; it may help to make some of this a little more clear.

[The prepared statement of Dr. Houk follows:]

Testimony by Dr. Vernon N. Houk

Mr. Chairman and Members of the Subcommittee:
I am Dr. Vernon N. Houk, Director, Center for Environmental Health, Centers for Disease Control (CDC), Public Health Service, Atlanta, Georgia. I am accompanied by Mr. Larry Edmonds, an epidemiologist on my staff.

I am pleased to represent the Public Health Service this morning to discuss CDC's birth defect surveillance activity and our involvement in the birth defect question in Midland County, Michigan.

CDC maintains two birth defect surveillance systems with a staff of eight persons. The Metropolitan Atlanta Congenital Defects Program (MACDP) began in October 1967 and is the more complete system because multiple intensive methods are used to identify infants with birth defects. These intensive methods include review of hospital records, records of local cytogenetic laboratories, and genetic counselling clinics, and of livebirth, infant death, and stillbirth certificates. Since its inception in 1967, this surveillance system, encompassing five Metropolitan Atlanta counties, with approximately 25,000 births annually, has registered some 15,000 infants with birth defects.

The Birth Defects Monitoring Program (BDMP), initiated in late 1974, is a surveillance system collecting data on diagnoses of birth defects in newborns from hospital discharge summaries from approximately 1,200 U.S. hospitals with obstetric services located in 750 counties in 45 States. This system contains data on 150 birth defect categories and includes approximately a million births per year. These 150 birth defect categories include individual malformations and grouped malformations covering the entire range of organ systems. Among these 150 are 37 categories we have selected as most helpful in identifying and analyzing national trends in major birth defects.

Data from the BDMP system are generally available for analysis within six months after the birth of the infant. Although this system is less complete than the MACDP, it is substantially more complete for those areas for which data are gathered than reporting of birth defects by birth certificate only. In some areas, the only birth defect information available to investigators is from birth certificates.

With the initiation of the BDMP system in 1974, we purchased existing data for 1970-1973. These data are used as baseline rates to compare with rates observed on new data acquired each succeeding year since 1974. These periodic reviews look for statistically significant increased rates in each defect category by county and other larger geographic areas. Analysis is performed as often as four times a year on this large volume of data. A statistically significant increase may occur by chance alone. For example, in the phrase "statistically significant at the 0.05 level", we mean that an event could have occurred by chance as many as 5 times out of one hundred. Therefore, these data must be interpreted cautiously.

CDC first learned of a possible increase in the incidence of birth defects in Midland, Michigan, when Mr. Todd Mason, a reporter for a Midland newspaper called Dr. J. William Flynt, at CDC, on March 29, 1976. Mr. Mason said he had data from birth certificates showing that the total malformation rates for Michigan (1970-1974) were 9/1,000 in contrast to 21/1,000 for Midland. Mr. Mason was concerned that these increases were due to vinyl chloride production in the Midland area. After discussing the problems of reporting variation and that the small numbers of birth defects could yield misleading results in interpreting birth certificate data, Dr. Flynt suggested that the next step would be to review the specific diagnoses on the birth certificates. Mr. Mason called on May 20, 1976, to say that the State Health Department had investigated the matter further and found that much of the increased incidence was due to better reporting of minor defects. However, for 1970-1974 the cleft lip and cleft palate rate was 26/10,000, about 3 times the rate reported on birth certificates for the entire State. Dr. Flynt pointed out that the rate was similar to and not significantly different from the rate (about 20/10,000) found from an intensive surveillance of birth defects in Metropolitan Atlanta for the same years. Mr. Mason also expressed concern that the birth defect incidence might be related to 2-4-5,Trichloro-phenoxyacetic acid (2-4-5,T), a herbicide produced in the Midland area.

In 1977, we were contacted by Ms. Jean Townsend, Epidemiologist, Michigan Division, Medical Department, Dow Chemical Company, who was planning a study of reproductive outcomes of employees of Dow in Midland. In June 1977, she was supplied with Birth Defects Monitoring Program data for Michigan and for the United States. In May 1978, at her request we supplied a list of severe birth defects. We further offered to objectively code defects into major and minor types without knowledge of the exposure status of the parents. We were not asked to do the coding.

In the fall of 1978, during our periodic review of BDMP data, we noted the increased rate of combined cleft lip and palate in the early 1970's for Midland County. In our judgment at the time of this analysis there was nothing particularly unusual about the increase observed in Midland. The annual incidence of several categories of birth defects by county varied significantly during these same years. It is important to remember that if one looks for increases for each of the 150 birth defects each year in a county, some increases will be observed due to chance alone.

In the Spring of 1979, Mr. Charles Poole, Epidemiologist, Epidemiology Branch, Office of Toxic Substances, Environmental Protection Agency (EPA), contacted Mr. Edmonds about Mr. Poole's desire to do a study of birth defects in Midland County. He was concerned about the possible association of birth defects and 2-4-5,T production at the Midland plant. CDC provided Mr. Poole suggestions about the proposed study design and encouraged him to work with the Michigan Department of Health. After several discussions with the concerned parties, Mr. Edmonds, Mr. Poole, and officials of the Michigan Department of Health met on November 19, 1979, to discuss Mr. Poole's protocol.

At the November 19 meeting, the study design that was discussed would have included, among other variables, the relationship between residence of the parents of children born with birth defects and proximity to the Dow plant. Similarly parental occupational exposures would have to be studied. It was agreed that the study had to consider exposure to all chemicals and not just to the single chemical 2-4-5,T and thus a revised protocol was needed. We consulted with EPA on the design of the study and encouraged EPA and the State of Michigan to work closely together because the issue of birth defects had been raised several times. We understood that a revised protocol would be forthcoming. Because we were serving as consultants and not as principal investigators, we took no action other than to encourage the principals to investigate this matter.

In 1981, CDC used BDMP data to do a State-by-State and county-by-county analysis of 37 CDC selected birth defects for live births from 1970-1980. These 37 defect codes were selected by CDC from the larger list of some 150 codes because we felt that they were the most appropriate codes to screen for increases in birth defects related to environmental, mutagenic, and genetic factors. In September 1981, the preliminary analysis was completed. We sent to each State Health Officer data for the United States as a whole. The data showed the annual frequency and rate of each defect. The letter offered State and county data if requested by the health officer. At the request of the Michigan Department of Health these data for all Michigan counties including Midland were given to Dr. Kenneth Wilcox, State Epidemiologist, Michigan Department of Health, in April 1982. For these 11 years combined (1970-1980) and 37 selected defect codes, there was only one significant increase for Midland County—dislocation of the hip, a condition with considerable inter-physician variance in diagnosis.

These 37 selected defects included a category for cleft palate alone and a category for cleft lip with or without cleft palate. This distinction was used, rather than all orofacial clefts combined, because in our opinion these two types of defects differ with respect to certain epidemiologic and genetic variables that suggest different etiologic mechanisms. If, however, the cleft palate alone and cleft lip with or without cleft palate are combined, the previously noted statistically significant increase for Midland County for the early 1970's is found. Table 1, included as part of this testimony, shows a total by year for 1970-1981 of the numbers and rates of the two defects alone and combined. You can see that for 1971, 1972, 1974, and 1975 there is between a 50% and 100% increase in combined orofacial defects when compared with the overall Michigan State rate. There is an unexplained increase between 1971 and 1975 in Midland County. The rates since 1975 have returned to expected levels.

The previously mentioned Townsend study of Dow Midland workers has now been published and raises additional questions about orofacial clefts. When one reviews the published report, though not discussed in the text, Table 3 of that report shows 10 infants with orofacial cleft defects among 2422 live births to wives of employees (1939-1975). This is twice what one would expect or a 2-fold increase in rate if these defects are combined.

In summary, for most categories of the 37 birth defects, we found no increases for Midland during the combined years of 1970-1981. The analysis of the 150 categories does show that during these twelve years the total reported combined orofacial clefts are elevated about 50% when compared with all of Michigan. This elevation occurs predominately because of increases in 1971, 1972, 1974, and 1975. In our opinion, these birth defect codes should be considered separately and not combined because the causal mechanisms for the birth defect may be different. We do not know the cause of the above increase in the frequency of combined orofacial clefts during these years or if there is a specific cause. It may never be possible to identify the cause, if any. CDC is available to provide technical consultation to the state of Michigan and others as appropriate.

Thank you, Mr. Chairman. I will be happy to respond to your questions.

Table 1

Centers for Disease Control
Birth Defects Monitoring Program
Incidence of Oral Clefts by Year Among Hospital Births
Midland County, Michigan, 1970-1981
(Rate per 10,000 Births)

Defect	Year	70	71	72	73	74	75	76	77	78	79	80	81	County Total 70-81	Michigan Total 70-81
Cleft Palate Alone	Number	1	2	1	1	2	1	0	1	1	0	2	1	13	670
	Rate	7.0	13.7	7.8	8.0	14.7	7.6	0.0	7.9	8.1	0.0	13.7	6.4	7.9	5.6
Cleft Lip +/- Cleft Palate	Number	1	5	3	1	3	3	2	1	1	0	0	1	21	1147
	Rate	7.0	34.2	23.5	8.0	22.0	22.8	15.1	7.9	8.1	0.0	0.0	6.4	12.8	9.5
All Orofacial Clefts	Number	2	7	4	2	5	4	2	2	2	0	2	2	34	1817
	Rate	14.0	47.9	31.3	16.0	36.7	30.4	15.1	15.7	16.2	0.0	13.7	12.9	20.7	15.1

Mr. SCHEUER. Thank you very much, both of you. Just as there is interphysician variance in diagnosis, I think my colleagues and I would agree that there is interparlimentary variance in political conclusions. That means politicians disagree sometimes just the way doctors do.

You have left us hanging sort of high and dry, Dr. Houk. What can you tell us about the impact of dioxin on the normal rate of birth defects and going from that what kind of research ought to be done and who should do it?

Dr. HOUK. Dioxin causes birth defects when fed to female animals and several species of mice and one species of rat. It causes other birth defects in other species of animals. In my opinion, sir, there is no study that is adequate to answer the question of whether dioxin causes birth defects in humans at this time.

Mr. SCHEUER. At our level.

Dr. HOUK. At any level in people. There are many people that will disagree with that but there are several studies, which in my opinion, are not valid, do not answer the question and are not appropriately designed, one of which is the famous Alsea study. It does not answer that question.

We are hopefully addressing this as part of the agent orange experience of Vietnam that we have a very large study going on 9,000 births from the metropolitan Atlanta birth defect registry looking for differences in the kinds of birth defects and whether the father served in Vietnam or did not serve in Vietnam. This only relates to the father and then hopefully some sort of dioxin exposure.

There needs to be a very adequate study, with a fairly large number of people, to answer this question in people. Very frequently we hear the liturgy of animal studies agreed to by all scientists in the group. The next statement that usually follows is, but that has not been shown to be true in humans. Though technically a correct statement, it is a very misleading statement because the correct and not misleading statement would be that the studies have not been done in humans.

Mr. SCHEUER. How large a population are you speaking of, this study that you recommend?

Dr. HOUK. I don't recommend a specific study now off the top of my head. The first thing is to get people who are exposed to significant levels. Then one has to look at the power that one would want to address this specific question, design a protocol, have it peer reviewed, see if it were possible to get enough people together to do the study. It certainly would not be possible to do it in a small population unless they are rather heavily exposed. Many of these things we are going to have to have by inference. Epidemiological studies never show cause and effect. We do the probability of cause and effect in association and try to exclude as many other things that are associated with that. Fortunately, we live in a country that in most of these instances we can never demonstrate conclusively cause and effect because that would mean exposing people purposely to these chemicals, which is unethical, and we cannot do it.

Mr. SCHEUER. In your opinion, could dioxin be the cause of the level of birth defects in Midland that are two or three times, according to that chart, the level experienced in the rest of the State of Michigan?

Dr. HOUK. There was a—I cannot give you a direct yes or no, if in fact there was an increase. In my opinion dioxin could be a cause of that increase. We are not certain that there is, in fact, an increase. During those 4 years in question there was about a 50-percent increase in the combination of cleft lip and cleft palates together. That may or may not have a cause. If it does have a cause we may or may not be able to find it by a very controlled and worked-up study.

One of the issues about reproductive outcome that is generally misunderstood, and I heard you ask the questions of several witnesses before about the 40 women in there and that would not be surprising. One would have to ask the following question at least: How were the wives selected? What were the outcomes that they asked for?

Mr. SCHEUER. How were they selected and by whom?

Dr. HOUK. By whomever asked the question. What were the outcomes they asked for? How were the outcomes confirmed? How many pregnancies they would have?

Let me give you an example why some of these questions are important. Just sheer numbers. The failure to conceive or infertility occurs in a frequency of about 15 percent in couples after 1 year of unprotected intercourse. Miscarriages occur in 16 to 20 percent of all pregnancies between the 8th and 28th week of gestation. Stillborns occur in 2 to 4 percent of all births. Birth defects identifiable within the first year occur in 3 to 5 percent of all births.

Birth defects identifiable within the first 15 years by very intensive ascertainment occurs in 15 percent of all births. So adverse reproductive outcome is not a rare, unusual, event as many people would like to have us believe when they talk about it.

Mr. SCHEUER. Thank you.

Congressman McGrath of New York?

Mr. MCGRATH. Thank you, Mr. Chairman. Thank you, gentlemen, for your testimony.

You seem to present us with a catch-22 situation where you cannot establish a standard for dioxin or any other toxic substance and yet you expect us to legislate against illegalities in the dumping of toxic wastes. I wonder how we can reconcile that.

Dr. HOUK. Birth defects. We were asked to prepare testimony primarily on birth defects in our involvement in Midland.

Birth defects are only one of the many documented adverse affects of dioxin in the animal model. Again, the correct statement is there are no acceptable human studies done as yet and the reason for that is because they are difficult and have not been done. There is no evidence that dioxin causes adverse human effect at the low level chronic concentration. But there is no evidence that it does not. Most of us believe, very strongly, that dioxin is a severely toxic chemical with very low chronic toxicity. I can't help but disagree with some testimony that you heard this morning. That in the absence of chloracne there is no possibility or the possibility is very remote that low-term dioxin contamination or exposure is not harmful. I believe the 99.99 percent of the scientific community who is not associated with industry would take exception to that statement.

Mr. McGRATH. What would the consensus be?

Dr. HOUK. The consensus would be that you do not need chloracne to predict long-term adverse health defects. One looks at the so-called Seveso incident exposure there. The concentration was a short-term exposure for relatively short periods of time. It is not surprising that there have been no malignancies because the time hasn't been long enough. Many of the malignancies that we are dealing with have 25-, 30-, 40-year latency periods. If you only study something for 10 years, it's not surprising that you don't see it.

Mr. McGRATH. Would it be fair to suggest that a compounding of an incidence of being exposed to dioxin would elicit a greater response as far as incidence is concerned of cancer or birth defects?

Dr. HOUK. Yes, Mr. Congressman. I believe very firmly, and there's not, and again this is a belief, there's not a lot of data, if we look at most toxic chemicals there are very few specific diseases caused by specific chemical compounds. Sarcoma of the liver, a special thing in the liver by polyvinylchloride. Asbestos—there's just a handful of these.

Most of the hazards just increase the risks of our normal diseases—heart disease, cancer, hypertension, liver disease. It doesn't take very much, particularly in liver and kidney, where some people might already be bordering on what is abnormal and normal. It does not take very much more to turn people to the distinct abnormal.

Another thing that we have to consider when we deal with this whole subject is that most of the biochemical tests that we have to measure bodily function, liver function, kidney function, have been developed since 1940. They have been developed since we have had massive chemicals in our environment. Though we may have what is population normative data, I'm sure that we do not have normal data. A case in point specifically, the normal blood lead of people, humans, approaches zero, and we can prove that. The mean blood lead level of children and adults in this country is around 15 micrograms per——

Mr. McGRATH. Dr. Poole, of the information that you examined from the statistics that were available to you, was there any consideration for those who spent more time working at that particular plant than those who spent less time?

Dr. HOUK. No. The excess—all we did—all we reported here is collecting the information for the excess.

What would have to be done to see if that would, if you could ferret this out, and it may not be possible to ferret it out right now, we go back to each of these birth defects with a control and do what is a case controlled study and see if one can find out if there are differences where the father's occupation, where they lived in the past, what sort of relationship he had. We must never forget the maintenance workers at the plant because they frequently are exposed to the highest levels. It is not only the engineers and the production people and so forth. The numbers are so small here that you might not be able to get an answer. It is worth a try. We would be willing to help try to do that. Not with the specific design of a study but several people sitting around the table would have to be working together to decide what is the most appropriate and what are the chances of having it done.

Mr. McGRATH. So in other words there really is no conclusive evidence as far as you are concerned, or you are concerned in your testimony that the incidence of dioxin in the soil or in the water in Midland, Mich., had a significant effect on the rate of birth defects?

Dr. HOUK. All we have are the birth defects that occurred in the Midland area plus the Dow study of the wives of Dow workers.

I don't know what the levels of dioxin in Midland, Mich., are. I don't know what the levels inside that plant are. I don't know what the avenues of exposure are. If one were going to do something one would have to get in, do those measurements, look at the avenues of exposure, look at health outcomes, find out if in fact that produces a significant hazard to the individual.

Even there the numbers may be too small. We have now as part of the Missouri dioxin investigation a fairly large number of individuals that we're putting into a registry and doing examinations and extensive laboratory work with.

A significant help here would be to combine, at least, some of those things and the people together so that we do get larger numbers of people to be able to answer these questions.

Mr. POOLE. We don't know presently whether dioxin had anything to do with the increase—apparent increase--in Midland, Mich., in the early seventies. The study I designed and have proposed, I think would go a long way in answering that.

I would say, though, at this time a study in Midland that would have to depend upon questionnaires or interviews would be subject to very extreme methodological criticism. In fact most epidemologists, I believe, would not recommend that an interview or questionnaire study be done in Midland at this time.

Fortunately, however, the occupational and residential questions could be answered using objective records and Dow Chemical has shown that it can identify when workers were in specific parts of its plants going way back into the 1930's. That could be done without the problems that the publicity has raised.

I'd also like to point out that I think a very misleading impression has been left that there is no solid human evidence on chronic health effects of dioxin. To the contrary, there is. The evidence on the association between soft tissue sarcoma, the rare form of cancer that Dr. Gehring mentioned, and exposure to dioxin is quite strong. Some studies he left out of his review of the literature, which go a long way toward supporting the studies that Dow Chemical themselves have done; they in Monsanto have followed workers who were highly exposed to dioxins and have shown a handful of these very rare forms of cancer. Such that even the experts that Dow Chemical had asked to look at the Swedish studies and who criticized them very severely, have now come around and believe that that evidence is very strong. So, it's my opinion, and I believe it's the opinion of most people who know all the data, that soft tissue sarcoma and dioxide is a very strong association. It's not certain to be causal, but it's a lot stronger, I think, than the testimony you have heard so far today would lead you to believe.

Dr. Houk. Mr. Congressman, could I say that I think the word suggestive is appropriate here. I believe that is being overstated, and I bring up that point because this directly impacts upon the agent orange problems of the veterans. I think suggestive is a more appropriate word than a very strong association. Now, it may change in a couple more years.

Mr. McGrath. Let me suggest something to you: that it is awfully difficult for us sitting up here to have as little information or as definitive conclusions as we need in order to make anything that we do or any standard that we set or you set or EPA sets stick legally. There's an old saying in politics: "No issue is black or white, all of it's sort of gray." But we can't vote maybe. That's sort of the situation that we're in here now. Unless we can come up with some real definitive concrete conclusion to some of the studies that you have ongoing at the present time, we're going to be hard pressed to make whatever standard that is set by the executive branch or legislative branch of government stick in law.

Dr. Houk. I believe the regulatory agencies—which we are not—could address this more fully than I can. I think that if we look historically for the past several decades, it is the policy of this government to use well conducted, well done animal/laboratory studies for the purpose of setting regulations in the absence of health information on humans to the contrary.

Mr. McGrath. I thank you.

Mr. Scheuer. I share my colleague's bepuzzlement and perhaps frustration. You yourself have said that there's a great deal of feeling in the scientific community that these laboratory animals do not necessarily reflect human reactions and the human experience. To what extent do you think we should regulate and ways that could be expensive to industry. Regulate dioxin, regulate phosphates. On the basis of animal laboratory experience and in the absence of the kind of long-term studies that you are talking about—human studies—what do we do in the meantime? Do we wait 10 or 15 or 20 years until the results of the study that you're in the process of designing and that EPA Chicago is in the process of designing, become available to us? Or do we say, although we don't know everything that doesn't mean that we can't do anything and that there is some minimum reasonable level of regulation that is justified by the animal experiments that have taken place up to date.

We want to be cost effective. We are trying to be effective competitors in global commerce. We cannot afford to lay unnecessary and nonproductive burdens on American industry. We've got to unleash them and enable them to do their thing and compete in global competition. On the other hand, we're concerned with the health of the American people. What level of regulation can we reasonably lay on industry, in terms of dioxin, justified by the animal experiments alone until the more definitive long-term human studies become available, perhaps in a decade or more?

Dr. Houk. Mr. Chairman, I think I would point out, as a way of answering that, that we were very successful in eradicating smallpox from this world before we knew everything about the smallpox virus.

You've had, I'm sure, biologic scientists many times in the past before you. If you ever waited for all of us to agree on any particular thing we'd probably be waiting a good long time.

I think that there are very prudent activities that need to be taken. If one has a chemical that has the potential of harm that dioxin does, at relatively low levels, then one must take a look very carefully at that. We recently made the recommendation to the Environmental Protection Agency that long-term exposure in soil in a residential situation to anything more than 1 part per billion dioxin constituted a health risk to individuals and that in turn made EPA, didn't drive their decision, but they used it in their decision process.

Those were based on a very carefully done health risk assessment, but using only animal data simply because there are no human data. If we wait for human data what may happen is that 50 years from now we may even have it. Many of our good epidemiologic studies, unless we tone our selection better, in 25 years may again have a definite yes, not a definite no, maybe.

We are trying to do things in my center in the laboratory to try to pick in groups of people who would be at higher risks and lower risks. Again, I remind you of the comment that you made and to reemphasize it. If we look historically at toxic chemicals—and what we know now as compared to what we knew 10 years ago—everything is worse now than it was then, and it makes us be on the very conservative end. You have a very difficult problem to make public policy in the absence of all the data. Yet, we cannot afford to wait until all of that data comes in.

Mr. SCHEUER. Are you familiar with Crohn's disease?

Dr. HOUK. Yes, sir.

Mr. SCHEUER. Can you tell us what it is and whether it might be related to dioxin and whether it's found in Midland County in higher percentages than in the rest of the country?

Dr. HOUK. I don't know its frequency in Midland County. I don't know what causes Crohn's disease. I'm not sure that anybody knows what causes the disease. Anything that is said to have 15 or 20 or 30 different causes and 15 or 30 different cures means that as a medical profession we don't know very much about it.

Mr. SCHEUER. Can you tell us just for the record what it is?

Dr. HOUK. It's a chronic inflammatory disease of a certain portion of the bowel. It's quite likely that it could have an environmental cause or at least be enhanced by environment. The same thing in all of the birth defects. These are all probably multifactorial diseases with some genetic background and then that is enhanced or added to by an environmental insult, by an environmental hazard, by an environmental chemical, by radiation, et cetera.

Mr. SCHEUER. Thank you very much, Dr. Houk. Before we adjourn, I'm going to ask unanimous consent that all members can submit questions in writing and that we hold the record open for 1 week or 10 days.

There being no objection so ordered.

We thank you very much for your testimony as well as for your patience in staying with us until after 4:30. Three and a half hours after we started the hearing.

The hearing is adjourned.

[Whereupon the subcommittee was adjourned, subject to the call of the Chair.]

APPENDIX

ADDITIONAL MATERIAL FOR THE RECORD

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
REGION V

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DATE: 1 MAY 1981

SUBJECT: Dioxin Report

FROM: Karl E. Bremer
Toxic Substances Coordinator

TO: Members of Dow Task Force

Please review the final draft of the Dioxin Report by Milt Clark for technical accuracy and offer comments no later than May 15, 1981. As this report will be released to the public it is extremely important that it be carefully reviewed. Thank you for your assistance.

cc: J. Lee/AHMD
D. Barnes
G. Amendola/SAD
V. Saulys/GLPO
B. Maddox/Water
C. Ross/SAD
T. McPhee/EWPE
T. Barney/EP
M. Mutman/EWPE
S. Gardeoring/E

[illegible] [illegible] [illegible]
language in your comments.
Thank you

A Review of Polychlorinated dibenzo-p-dioxins (PCDDs) and Polychlorinated dibenzofurans (PCDFs): Sources and Effects

Prepared by:

J. Milton Clark, Ph.D.
Health Effects Specialist
USEPA Region V Office of Toxic Substances

I. Introduction

In the last several years, concern over the environmental and public health effects from the use of 2,4,5-Trichlorophenoxyacetic acid (2,4,5-T), a herbicide, has increased. Chemical products with 2,4,5-T were shown to contain a trace contaminant 2,3,7,8-Tetrachloro-dibenzo-p-dioxin (TCDD). This chemical, commonly known as dioxin, is possibly the most toxic chemical synthesized by man. Many commercial products contain chlorinated dioxins, technically known as polychlorinated dibenzo-p-dioxins (PCDDs) and related compounds, polychlorinated dibenzofurans (PCDFs). Evidence exists that PCDD and PCDFs may also be released to the environment by combustion processes. This report (1) summarizes the sources of PCDDs and PCDFs; (2) lists the physical, chemical, and biological properties of these compounds; and (3) discusses those studies involving PCDDs and PCDFs in the Great Lakes area.

II. Sources of Polychlorinated dibenzo-p-dioxins (PCDDs) and dibenzofurans (PCDFs) in Commercial Products

A. 2,4,5-T (phenoxy acids)

The dioxin problem was first observed in connection with the teratogenic effects observed in laboratory animals from 30 ppm of TCDD in the herbicide 2,4,5-T (1). TCDD is formed in the manufacture of 2,4,5-T from 1,2,4,5-tetrachlorobenzene, especially if production temperatures exceed 160°C(2). Drums of Agent Orange stored in the USA and in the Pacific prior to 1970 have been reported to have TCDD levels ranging from 0.1 to 47 ppm (3). Only trace levels of other PCDDs and PCDFs were found. Currently, producers of 2,4,5-T claim that their products contain less than 0.1 ppm of TCDD (2). On February 28, 1979, the use of 2,4,5-T and Silvex containing products was immediately suspended due to findings of increased spontaneous abortions in Alsea, Oregon, an area where 2,4,5-T had been extensively used in forestry to control undesirable plant growth. (4,5). This study has since been discredited.

B. Chlorinated Phenols

PCDDs and PCDFs have been found in tri, tetra, and pentachlorophenols. The quantities of these compounds and their isomeric forms depend upon the reaction process and conditions. Current concentrations of 2,3,7,8-TCDD in 2,4,5-trichlorophenol (2,4,5-TCP) and its sodium salt are less than 0.1 ppm (6). Analyses of PCDDs in commercial grade pentachlorophenols (PCP) produced by by various manufacturers during the years 1975 to 1977 found hexa-CDDs (HxCDDs) [non-detectable(N.D.) to 520 ppm], hepta-CDDs (HpCDDs) (125 to 130 ppm) and octa-CDDs (OCDDs) (N.D. to 3600 ppm) (7). No TCDD was found in commercial PCP. PCDFs were also detected including hexa-CDFs (HxCDFs) (9 to 90 ppm), HpCDFs (70 to 400 ppm) and OCDDs (55 to 260 ppm). There are several isomeric forms of HxCDD, the major isomers being the 1,2,3,6,8,9 (40-50%); 1,2,3,6,7,8 (20-40%); and 1,2,4,6,7,9 (20-40%). The isomeric forms for HpCDD are 1,2,3,4,6,7,9 (60%) and 1,2,3,4,6,7,8 (40%). Commercial PCP also contains 5-10% tetrachlorophenol and about 5% of various chlorinated phenoxy phenols.

III. Sources of PCDDs and PCDFs from Pyrolysis, Combustion and Photolysis

A. Formation of PCDDs by Pyrolysis of Chlorinated Phenols

1. The burning of materials impregnated with commercial 2,3,4,6 tetrachlorophenates yielded a total of 150-1000µg of PCDDs/kg of chlorophenate. The PCDD isomers detected ranged from various TCDDS to HpCDDs. The 2,3,7,8 TCDD and 1,2,3,7,8 penta-CDD (PnCDD) isomers were both present as minor constituents (3,8).

2. The pyrolysis (burning) of penta and 2,4,6-trichlorophenate yielded only 1,3,6,8 and 1,3,7,9 TCDD isomers (3,8).

3. Only trace amounts, if any, of 2,3,7,8-TCDD are formed by thermal reactions of the phenoxy acid 2,4,5-T (9).

B. PCDDs and PCDFs in Fly Ash and other Combustion Sources

1. Total amounts of PCDDs and PCDFs in fly ash from a municipal incinerator in Switzerland were found to be 0.2 ppm and 0.1 ppm respectively. At an industrial heating facility, the fly ash contained 0.6 ppm PCDD and 0.2 ppm of PCDF were found. The highly toxic PCDDs (2,3,7,8; 1,2,3,7,8; 1,2,3,6,7,8) were the predominant isomers found (3).

2. A study released by Dow Chemical in 1978 and published in 1980 (10) reported no 2,3,7,8 TCDD (10 ppb detection level) in fly ash from their oil and coal power plant; however, 38 ppb of other TCDD isomers were found at a detection limit of 20 ppb. Dow also reported finding detectable levels of PCDDs from fireplaces, automobile and truck mufflers and cigarette smoke. Dow concluded that dioxins have been present since the advent of fire. The results of their study are presented in Table 1 on page 4.

In contrast to Dow's 1978 report, the authors tempered their remarks in this more recent report by stating that some combustion sources may be sources of airborne and waterborne particulates containing PCDDs. ~~The~~ The formation of PCDDs was attributed partly to the reaction between inorganic chloride and organic material and not due to the condensation of preexisting polychlorinated phenols.

3. Kimble and Gross (11), in contrast with Dow Chemical findings, concluded that coal fired power plants were an insignificant source of TCDD.

TABLE 1

Dow Chemical's Findings on PCDDs and PCDFs
In Fly Ash and Other Combustion Sources (Reference #10)

Sample	Number of samples	Apparent dioxin content, ng/g(ppb)					
		TCDD					
		Other isomers	2,3,7,8-	Total	HxCDD	HpCDD	OCDD
Incinerators, powerhouse							
Dow powerhouse	1	38(20)	N.D.(10)	38(20)	2	4	24
Dow rotary incinerator stack (present normal operation with supplemental fuel)	5			N.D.(2)	1-5	4-100	9,950
Dow stationary tar burner stack (normal operation with supplemental fuel)	5	N.D.	N.D.	N.D.	1-20	27-160	190-440
U.S. municipal incinerator (electrostatic precipitator)(Nashville, TN)	1	7.3	0.4	7.7	14	28	30
European municipal incinerators				2-20	30-200	60-130	40-12
Mufflers							
Diesel truck muffler	2	0.02	0.003	0.023	0.020	0.100	0.26
Auto muffler	4	N.D.-0.004	N.D.-0.004	N.D.-0.008	N.D.	0.003-0.01	0.02-
Other sources							
Home fireplace soot	2	N.D.-0.3	N.D.-0.1	N.D.-0.4	0.2-3	0.7-16	0.9-2
Home electrostatic precipitator	1	0.4(0.4)	0.6	1.0	34	430	1,300
Cigarette smoke	2	N.D.	N.D.	N.D.	0.004-0.008	0.009	0.02-
Charcoal-broiled steak	4	N.D.	N.D.	N.D.	N.D.	N.D.	0.03(

Where multiple samples were analyzed from similar sources, the range of observed values i
shown. 2) N.D. indicates that the signal observed was less than 2.5 times noise. Limits
detection not within these ranges are shown parenthetically after the value reported for
nals between 2.5 and 10 times noise. 3) Data without supplemental fuel is not included
because this practice has been eliminated.

No TCDD was detected at a detection limit of 1.2 ppt in fly ash. The authors concluded that the conversion of less than 1 x 10^{-10} of the chloride in coal would be converted to TCDD. The authors concluded that this reaction would be insignificant.

C. Formation of PCDFs by Pyrolysis of PCBs

1. The pyrolysis of commercial PCBs (Aroclor 1254 and 1260) at temperatures of 500-600°C has been shown by Rappe and his co-workers to yield 30 major and more than 30 minor PCDFs. From 3 to 25% of the pyrolyzed PCB was converted to PCDFs. One of the major constituents was 2,3,7,8-TCDF, the most toxic PCDF. Above 700°C only trace amounts of PCDFs are formed due to the complete destruction of PCB. The formation of PCDFs was shown to be the result of intermolecular cyclizations of PCB (12).

D. Formation of PCDDs by Photolysis

Dechlorination of OCDD in pentachlorophenol will produce tetra, penta, hexa, and hepta chlorinated dioxins. Only the 1,4,6,9-TCDD isomer is produced; the highly toxic 2,3,7,8-TCDD is not (7).

IV. Properties of PCDDs and PCDFs

The majority of information on PCDDs has been confined to the 2,3,7,8 isomer of TCDD. Because of structural similarities, the other PCDDs and PCDFs would be expected to have similar properties. A summary of the properties of TCDD is provided below (2,14).

A. Physical Properties

TCDD is a non-volatile, white crystaline solid with a melting point of 302-305°C. Water solubility is very low, being about 0.2 µg/l. The solubility of DDT in water is 1.2 µg/l. The compound binds very strongly to soils such as clays and loams. Temperatures in excess of 500°C are required for decomposition. UV light and sunlight have been shown to readily degrade TCDD if the TCDD is not bound to soils.

B. Environmental and Biological Properties

TCDD, at concentrations from 1 to 100 ppm, is persistent in the environment with an apparent half life of greater than one year. Because TCDD is highly lipophillic, it readily bioaccumulates. Laboratory aquatic tests with TCDD added to soils indicated bioaccumulation throughout simulated aquatic food chains with bioaccumulation factors as high as 26,000 times. In mammalian studies TCDD is poorly metabolized and eliminated primarily in the feces.

V. Summary of Toxicological Effects of PCDDs and PCDFs in Animals

Extensive toxicological reviews of the health effects of PCDDs and PCDFs have been presented elsewhere (2,6,7,13,14). A brief summary of the toxicological findings, extracted from these reviews, is presented below.

A. TCDD

1. LD50

The LD50 for 2,3,7,8-TCDD has been shown to be as low as 0.6 µg/kg-body weight (bw) (guinea pigs) in the animal species tested.

2. LC50

The approximate LC50 for coho salmon exposed for 96 hours to 2,3,4,8-TCDD and kept under observation for 60 days was 0.005 µg/l. Mortality was observed at concentrations as low as 0.056 ng/l.

3. Subchronic and Chronic Studies

Doses as low as 0.1 ng/kg-bw have been shown to cause liver degeneration in rats. Daily oral injection of 1 µg/kg-bw of 2,3,7,8-TCDD has been reported to be lethal to young rhesus monkeys. Death, physiological effects and hormonal alterations have been noted at dosages as low as 0.01 µg/kg-bw/day in feeding studies involving rhesus monkeys (15). Physiological effects included weight loss, loss of facial hair, gangrenous necrosis of the terminal phalanges, acneform eruptions, anemia, epidermal and internal hemorrhages of major organs, and bone marrow and lymphoid hyperplasia.

4. Fetotoxicity and Teratogenicity

2,3,7,8-TCDD has been shown to be fetotoxic and teratogenic at doses as low as 0.01 µg/kg-bw/day. Embryomortality, cleft palate, and kidney abnormalities have been observed in fetuses of rats, mice, and hamsters. Female Rhesus monkeys have exhibited reduced fertility and abortions at feeding levels of 0.01 µg/kg-bw/day (16).

5. Carcinogenicity

In long-term feeding studies with rats, TCDD has been reported to be carcinogenic at levels as low as 0.1 µg/kg-bw/day.

B. Other Chlorinated Dioxins (PCDDs)

Of the six chlorinated dioxins found in pentachlorophenol, two (1,2,3,7,8,9 and 1,2,3,6,7,8) would be expected to have marked toxicity given that the 2,3,7,8 positions are halogenated (7). In fact, these PCDDs are the only two HxCDDs which have been studied. The LD50 is respectively 60 and 100 µg/kg in guinea pigs. However, only trace levels of the 1,2,3,7,8,9 isomer are found in PCP. Chronic studies have determined that a mixture of these two isomeric dioxins at doses as low as 10 µg/kg/day were highly lethal to rat fetuses during late gestation. Subcutaneous edema of the fetuses were observed at 1 µg/kg/day while a 0.1 µg/kg dose did not yield any fetal anomalies.

Studies on the HpCDD of probable highest toxicity (1,2,3,4,6,7,8) with guinea pigs discovered relatively low toxicity of the compound with a single oral dose of 180 µg/kg. Further studies are currently in progress at NIEHS. In the limited studies conducted with OCDD, oral doses of 4 g/kg did not cause death in male mice. In a teratology study, no signs of maternal toxicity or fetal anomalies were observed in rats that received 500 mg/kg-bw/day of OCDD.

C. Polychlorinated Dibenzofurans (PCDFs)

From the limited studies conducted to date on PCDFs which are predicted to have the highest toxicity (2,3,4,7,8 and 1,2,3,6,7,8), the 2,3,4,7,8 dibenzofuran showed significant toxicity. In guinea pigs, 100% mortality was observed with a single oral dose of 10 µg/kg. Enlarged livers were noted upon sacrifice 30 days after a single dose of 1 µg/kg.

VI. Summary of the Toxicological Effects of PCDDs and PCDFs on Humans

A. Human Exposure from Industrial Accidents

There have been a number of industrial accidents during the manufacture of chlorinated phenols that have resulted in human exposure to TCDD (2,13). The more noteworthy are presented below:

1. Nitro, West Virginia (1949). An explosion at a 2,4,5-T chemical plant led to 228 cases of chloracne among exposed workers. Symptoms included shortness of breath, intolerance to cold, palpable and tender liver, loss of sensation in extremities, fatigue, nervousness, irritability, insomnia, loss of libido, and vertigo.

2. Germany, 1953. An accident at a 2,4,5-TCP plant caused 42 persons to have serious dermatitis, 14 of whom developed damage to internal organs, and 7 experienced nervous system disturbances.

3. Germany, 1954. Thirty-one workers at a 2,4,5-T plant suffered from chloracne and experienced various psychological symptoms. Researchers tentatively identified the causative agent as TCDD.

4. United States (1964). At a 2,4-D and 2,4,5-T plant, 11 of 29 workers developed chloracne and porphyria cutanea tarda (liver damage).

5. Derbyshire, England (1968). An explosion at a 2,4,5-TCP plant caused 79 cases of chloracne, many of them severe, among workers.

6. Seveso, Italy (1976). An accident at a chemical plant released approximately 2 to 10 pounds of TCDD over a wide area. Hundreds of animals died, and many area residents (in excess of 100) had confirmed cases of chloracne. Reports of increased spontaneous abortions have not been confirmed. Recent reports have confirmed that cow milk samples collected in 1976 near the explosion area had TCDD levels approaching 8 ppb (17). Rabbit liver samples were found to contain ppb levels of TCDD (18).

B. Human Exposure From Waste Oil and 2,4,5-T

1. Missouri (1971). A major poisoning episode affected humans, horses, and other animals. Waste oil, containing TCDD, had been sprayed on riding arenas to control dust. Within days, birds were found dead on the arena floor. Of 85 horses exercised within the arena, 62 became ill, and 48 died. Horses died over a period of 2 1/2 years. Human symptoms were less severe, but one 6 year old child, who played in the arena, developed hemorrhagic cystitis.

Analyses of soil samples from the arena showed the presence of TCDD ranging from 31.8 to 33.0 ppm.

2. Alsea, Oregon (1979). In 1978, the U.S. EPA, in conjunction with local and state health officials, began to investigate spontaneous abortion rates, in response to local complaints. Eight women living in the area claimed to have experienced 10 miscarriages since 1973. The area where the women were located was forested land which had been sprayed for years with 2,4,5-T. A study of six year abortion rates concluded: (1) that women residing in the area where 2,4,5-T usage was extensive, had a statistically higher rate of abortions than than women residing in two control areas (one rural, one urban), (2) that significant correlation existed between the pounds of 2,4,5-T applied and the rate of spontaneous abortion after a lag time of 2 or 3 months; and (3) that there was a statistically significant seasonal cycle in the abortion index, with the highest peaks in June. These findings led to the immediate suspension of 2,4,5-T usage in 1979 (4). Although these data do not prove a cause and effect relationship, they are believed to highly suggestive (40).

3. Australia (1979)

A strong correlation was noted with the use of 2,4,5-T and the frequency of birth defects involving the brain or spinal column (41).

VII. Studies Involving PCDDs and PCDFs Conducted in the Great Lakes Area

A. Dow Chemical Monitoring Study, Midland, Michigan (June, 1978)

In June, 1978, Dow Chemical reported results of their monitoring program to the Michigan Department of Natural Resources, as requested by that agency (19). The data has been summarized on the following page.

1. Tittabawassee River Water and Sediment (1976)

Ten samples (two water and eight sediment) from the Tittabawassee River above and below the plant showed no detectable amounts of TCDD. The detection limit (DL) for sediments ranged from 10 to 50 ppt. Water samples were analyzed at a DL of 1 ppt.

2. Plant Discharge Stream (1976-1978)

Composite and "grab" samples of wastewater discharge revealed no detectable levels of TCDD in 13 of 14 samples (DL 5 ppt or less). One sample was found to contain 8 ppt of TCDD.

3. Bioconcentration Study (1978)

Analyses of caged fish (trout) placed six miles downstream, for periods of 7 to 30 days, revealed no detectable levels of TCDD at a LD of 20 ppt. However, the 30 day trout analyzed with more sensitive methods revealed TCDD at levels ranging from 10 to 20 ppt.

Five of six fish placed in the tertiary pond for 7 days were found to have levels of TCDD ranging from 30 to 50 ppt.

4. Native Fish Studies

1976

TCDD was detected in 4 of 9 catfish samples at levels ranging from 70 to 230 ppt. Three of the four samples in which TCDD was detected were located downstream of Dow's chemical effluent. OCDD was found in 8 of 9 fish, collected both upstream and downstream of Dow's discharge. The levels ranged from 40 to 150 ppt. One fish sample was positive for HxCDD (90 ppt). Detection limits ranged from 10 to 200 ppt.

1977

Fish caught downstream of Dow at Smith's Crossing in the Tittabawassee River revealed contamination in 9 of 14 fish tested. TCDD levels ranged from 20 to 244 ppt.

Saginaw Bay, 1978

Of three fish collected from Saginaw Bay, one (catfish) was found to contain 24 ppt TCDD, at a DL of 10 ppt.

5. Chlorophenols

Chlorophenols were found in the Dow effluent up to levels of 70 ppb. 2,3,4,6-TCP and PCP were present at ppb levels below Dow's dam sediments of the Tittabawassee River. All the above mentioned chloroophenols were found in fish at ppb levels below Dow's dam. Pentachlorophenol was detected in fish above Dow's waste water stream.

Based upon these findings by Dow Chemical, EPA concluded that widespread environmental contamination of PCDDs existed. Since this represented a substantial risk, EPA requested further refinement of the data supplied to Michigan DNR. EPA also concluded that Dow's discharge represented the major source, if not the only source of TCDD contamination found in the Tittabawassee and Saginaw Rivers and Saginaw Bay in Michigan (20,21).

B. Dow Chemical Monitoring Study, Midland, Michigan (October, 1978)

Results of PCDD sampling conducted on Dow's waste streams indicated the presence of 2,3,7,8-TCDD in the 2,4,5-T sludge at 10 ppt and in trichlorophenol scrubber fluid at 20 ppt (22). The 2,4,5-T sludge also contained 11 ppt HxCDD, 4 ppt HpCDD, and 43 ppt OCDD. Brine wastes and sludges from 2,4-D processes were negative for PCDDs.

C. U.S. EPA TCDD Fish Monitoring Program (December, 1973)

In response to Dow Chemical's monitoring report, which indicated incidental contamination of fish from the lower Tittabawassee River, fish were collected and analyzed from the Tittabawassee, Grand and Saginaw Rivers (23). Twenty-six out of 35 fish samples contained detectable levels of TCDD ranging from 4 to 695 ppt. Eleven of these fish samples contained TCDD levels greater than 40 ppt. All but two of these samples were from locations downstream of Dow Chemical Company. Four out of 6 samples collected upstream were found to be negative for TCDD. Data is presented in Table 2 on pages 14 and 15. Analyses of blind controls, which consisted of various known levels of TCDD, indicated that the positive results may be viewed with confidence and within 20% of the values reported. The analytical method utilized did not distinguish between isomeric forms of TCDD. Three other isomeric forms of TCDD, besides the highly toxic 2,3,7,8 were noted.

Based upon a review of these findings, the FDA advised a tolerance limit of 100 ppt in fish. Where PCDDs had been found in fish below 100 ppt, it was recommended that no more than one average size portion of fish be consumed per week (24).

D. U.S. EPA Monitoring Study of Dow Chemical, Midland, Michigan (April, 1979)

Results of TCDD analysis of samples taken from Dow's 2,4,5-Trichlorophenol injection well (60×10^{-15} detection limit), phenol treatment system (82 ppt DL), Dow's effluent (2×10^{-15} DL), and upstream Tittabawassee River (50×10^{-18} DL) were found to be negative (25). However, the carbon

TABLE 2

RESULTS OF 2,3,7,8-TETRACHLORODIBENZO-P-DIOXIN
(TCDD) FISH MONITORING PROGRAM CONDUCTED BY
THE U.S. ENVIRONMENTAL PROTECTION AGENCY
IN MICHIGAN DURING 1978

Tittabawassee River				
Tittabawassee Road	Carp	42.2	52	8
	Yellow Perch	16.2 11.0b	20	8
	Carp	39.7	93	6
Freeland Road	Carp	40.0	32	4
	Yellow Perch	16.8 12.3	10	5
Smith's Crossing Road	Channel Catfish	50.3	273	6
	Carp	38.0	22	11
	Channel Catfish	38.2	695	60
	Carp	23.1	49	1
	Sucker	35.6	8	4
	Sucker	38.1	21	4
Above Dow Dam	Channel Catfish	30.9	42	9
	Carp	34.6	NDc	5
	Carp	33.0	ND	9
	Channel Catfish	38.1	28	2
	Yellow Perch	19.3	ND	4
Dublin Road	Carp	52.2	ND	9

TABLE 2 (cont'd)

Saginaw River				
Wickes Park	Carp	46.0	62	1
	Yellow Perch	11.9 11.4	ND	1
Block's Marina	Channel Catfish	69.0	105	7
	Channel Catfish	48.5	52	8
	Carp	51.8	28	4
Mouth	Channel Catfish	46.0	30	6
	Carp	45.0	153	1
	Yellow Perch	16.0 16.0	11	4
Grand River				
Jones Road near Eagle	Carp	39.0	20	4
	Carp	39.0	41	8
	Channel Catfish	----	29	6
	Smallmouth Bass	35	7	6
	Smallmouth Bass	38.0	8	6
Near Ionia	Carp	50.8	ND	2
	Sucker	48.3	ND	2
Saginaw Bay				
Lat. 43 40' 16"	Sucker	28.2 31.0	4	2
Long. 83 50' 21"	Yellow Perch	24.2 26.8	ND	3

TABLE 2 (cont'd)

Location	Fish Species	Fish Length (cm)	TCDD Level (ppt)a	TCDD Dectect Limit (ppt
Lake Michigan				
Off Saugatuck	Lake Trout	50.8	ND	7

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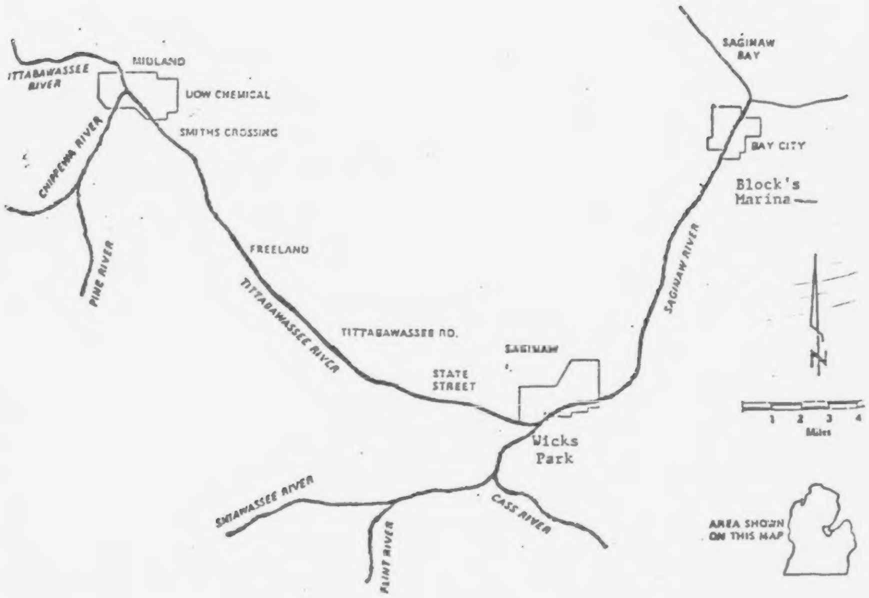
a ppt indicates parts per trillion which is equivalent to ng/kg.

b signifies composite fish sample.

c ND indicates that TCDD was not detected in the fish sample at the corresponding detection limit.

SAGINAW RIVER BASIN


ITTABAWASSEE RIVER
MIDLAND
DOW CHEMICAL
SMITHS CROSSING
CHIPPEWA RIVER
PINE RIVER
FREELAND
TITTABAWASSEE RIVER
TITTABAWASSEE RD.
SAGINAW
STATE STREET
Wicks Park
SHIAWASSEE RIVER
FLINT RIVER
CASS RIVER
SAGINAW BAY
BAY CITY
Block's Marina
SAGINAW RIVER
N
1 2 3 4
Miles
AREA SHOWN ON THIS MAP

filter concentration system utilized was believed to be unsuitable for concentrating contaminants water samples.

E. Composite Fish Sample from the Tittabawassee River (December, 1980)

A single composite fish sample of five carp, supplied by the MDNR, (collected downstream of Dow Chemical) and analyzed by Columbia National Pesticide Laboratories, yielded positive results for various PCDDs and PCDF's. The 2,3,7,8 isomer of TCDD predominated (26).

The results are shown below:

	ppt Detection Level		ppt Detection Level
TCDD	81	TCDF	37
PCDD	31	PCDF	73
HxCDD	44	HxCDF	145
HpCDD	53	HpCDF	31
OCDD	14	OCDF	4
Total PCDD	223	Total PCDF	290

do these include TCD, HxCD, Hpc etc?

F. Dow Chemical Monitoring Study, Midland, Michigan (October, 1980)

In October, 1980, Dow Chemical published a report on environmental sampling for chlorinated dioxins (10). Included in this report were data from analyses of soils, dusts, and emissions from a rotary kiln incinerator, collected between 1976 and 1978. These sites were located within the Dow Chemical facility. The results, presented in Table 3 on page 20, (given in ppb) clearly shows that the highest levels of PCDDs in soil and dust samples were those collected at Dow Chemical. One soil sample was found to contain 100 ppb of 2,3,7,8-TCDD. OCDD was found at levels as great as 20,000 ppb. Particulate matter collected from a rotary kiln incinerator, operated without supplementary fuel and burning wastes from the facility, had levels of total TCDD reaching 14,000 ppb (see Table 4 on page 18). ~~Mention is made that~~ results from the particulate analyses ?

Particulates collected from the scrubber water contained TCDD at levels up to 2,500 ppb when the kiln was operated without supplementary fuel (see Table 5 on page 19).

G. Canadian Study on Gull Eggs from the Great Lakes

Dr. Douglass Hallet of the Canadian Wildlife Service reported finding 2,3,7,8-TCDD in Herring gull eggs, collected in 1980, at 12 different locations within the Great Lakes (27). The highest levels of TCDD were found in Saginaw Bay (43-90 ppt). Levels in Lake Ontario eggs were slightly lower and ranged from 44-64 ppt. Trace levels (approximately 3-10 ppt) were found in eggs collected at other Great Lakes sites. There have been no reports of abnormalities in gull chicks or mature birds. The 2,3,7,8-TCDD isomer was the only one detected in Herring gull egg samples at all locations. Egg samples collected from Lake Ontario in 1971 had TCDD levels of 300 ppt. These results indicate a decrease in TCDD levels and may be the result of Hooker Chemical discontinuing production of 2,4,5 Trichlorophenol in 1971. Confirmational analyses of samples are now underway in U.S. laboratories. Preliminary analyses from the University of Nebraska indicates that total TCDD results are about 10 fold greater than those found in the Canadian study, probably due to the use of a different recovery method and reporting the data corrected for losses during recovery (28).

H. Gull Flesh Analyses From the Great Lakes (December, 1980)

Two flesh samples from gulls in the Saginaw Bay were recently analyzed by Dr. David Stalling of the Columbia National Fisheries Research Laboratory (19). In the two samples, the 2,3,7,8 TCDD isomer predominated and was

Chlorinated Dioxins in the Environment (Reference #10)

	Number of samples	Apparent dioxin content. ng/g (ppb)[1]					
		TCDD					
		Other isomers	2,3,7,8-	Total	HCDD	H CDO	OCDD
Soil							
Rural (Gaylord, MI)	5			N.D.[2]	N.D.	N.D.-0.05	N.D.-0.2
Urban (Lansing & East Lansing, MI)	5			N.D.	0.03-1.2	0.03-2	0.05-2
Major metropolitan (Chicago, IL)	8			0.005-0.03	0.03-0.3	0.1-3	0.4-22
Dow Chemical (Midland, MI)	5	0.8-18	0.3-100	1-120	7-280	70-3,200	490-20,00
Dust							
Dow Chemical lab.	6	0.5-2	0.7-3	1-4	9-35	140-1,200	650-7,500
Midland, Michigan	2			0.03-0.04(0.02)[3]	0.2-0.4	2-4	20-30
Metropolitan (Detroit, MI)	4			N.D.-(0.03)	N.D.-0.3	0.3-4	0.1-4
Metropolitan (St. Louis, MO)	1	0.16	0.12	0.3	2	34	210
Metropolitan (Chicago, IL)	2			0.04(0.04)	N.D.-0.3	0.6-3	3-8

1. Where multiple samples were analyzed from similar sources, the range of observed values is shown.
2. N.D. = Not Detectable
3. Value in parentheses indicates detection limit.

Chlorinated Dioxin Content of Particulate Matter

From the Rotary Kiln Incinerator

Reference #10

	Fuel[1]		Apparent dioxins, ng/g (ppb)				
			TCDD				
Sample	Kiln	Secondary	Other isomers	2,3,7,8-	HCDD	H_7CDD	OCDD
			Without supplemental fuel				
R_1F_1	T,SW,G	T	1,800	2,800[2]	13,000	110,000	180,000
R_1F_2	T,SW,G		5,000	8,200[2]	65,000	510,000	810,000
R_2F_1	T,SW,G		3,300	110	1,300	2,000	3,000
R_3F_1	T,SW,G		12,000	N.D.(260)[3]	5,600	37,000	59,000
			With supplemental fuel				
R_3	T,SW,G	O,G	N.D.(8.0)	N.D.(2.0)	1.4	13.0	30.0
R_4	T,SW,G		N.D.(7.0)	N.D.(5.0)	N.D.(1.0)	4.0	9.0
R_5	T,SW,G		N.D.(2.0)	N.D.(2.0)	N.D.(0.5)	6.0	15.0
R_6	T,SW,G	T,G	N.D.(2.0)	N.D.(4.0)	5.0	27.0	170.0
R_7	T,SW,G		N.D.(2.0)	N.D.(2.0)	4.0	110.0	950.0

1. T, tars; SW, solid waste; G, gas; O, oil.

2. The high results reported for the 2,3,7,8-isomer are probably due to analysis by the nonspecific GC-MS packed-column method. Later results were obtained with a capillary column specific for 2,3,7,8-TCDD. The TCDD results from run 1 (R_1) are not comparable to those from runs 2 and 3.

3. Numbers in parentheses are limits of detection.

TABLE 5

Chlorinated Dioxins in Rotary Kiln Incinerator Scrubber Water

Reference #10

Sample	Apparent dioxins, ng/g (ppb)				
	TCDD				
	Other isomers	2,3,7,8-	HCDD	H_7CDD	OCDD
Particulates filtered from scrubber water					
Without supplemental fuel	300	2,200*	3,400	26,000	42,000
With supplemental fuel	14	32*	200	970	1,200
Filtered scrubber water without supplemental fuel	0.0018(0.01)	0.001*(0.0006)	0.005	0.024	0.026

* The analytical method did not separate 2,3,7,8-TCDD from 11 other isomers.

found at levels of 70 and 160 ppt. HxCDD and OCDD were also found resulting in a total PCDD level of 136 and 196 ppt. Total PCDFs were found at 117 and 121 ppt with the PnCDF and HxCDFs being the predominate furans. The 2,3,7,8--TCDD levels have been confirmed within experimental error by the U.S. EPA Research Triangle Park laboratory and by Buser of Sweden.

I. PCDDs Analyses on Great Lakes Fish (April, 1980)

The Columbia National Fisheries Research Laboratory has obtained preliminary, positive results for TCDD, on composite fish samples from the Great Lakes (30). This fish sampling is being conducted under the National Pesticides Monitoring Program. Both Huron and Ontario fish range in TCDD concentrations from 33 to 160 ppt. The highest values were reported to fish collected from Saginaw Bay. TCDD was not detected in fish from Erie and Lake Superior. The predominate isomeric form of TCDD discovered has been 2,3,7,8-TCDD. Data collected to date is presented in Table 6, pages 24 and 25. The New York State Department of Health is currently screening Lake Ontario fish for TCDD contamination. Previous analyses conducted by the agency determined TCDD contamination at about 10 ppt. Fish samples collected below the Niagra River had no detectable levels of TCDD. Sediment samples taken from streams in the vicinity of Hooker Chemical, where 2,4,5-TCP wastes were dumped, have been reported to be positive for TCDD (31).

J. NIEHS Analyses of a Michigan Dairy Herd Tissue Samples and Michigan's Study on Pentachlorophenol Treated Wood (1978-1979)

Studies by NIEHS of a dairy herd in Michigan, presumed to be contaminated by contact with PCP treated wood, revealed fat and liver contamination, respectively, with OCDD at 7 and 15 ppb; HpCDD at 6 and 15 ppb; and HxCDD

TABLE 6

Residues of Dibenzofurans and Dibenzo-p-dioxins in Composite Samples of Fish and Gulls From Different Sites on the Great Lakes. Residues are in parts-per-trillion and by Number of Chlorine Substitutions.

Site and Sample	Dibenzofurans 4Cl	5Cl	6Cl	7Cl	8Cl	Total	Dibenzo-p-Dioxins 4Cl	5Cl	6Cl	7Cl	8Cl	Total	Sample Index No.
Saginaw Bay, L. Huron Carp	27	44	34	44	4	153	94	157	122	12	ND	385	GL1
Saginaw Bay, L. Huron Herring Gull #1	16	28	57	17	3	121	160	ND	20	ND	19	199	GL2
Saginaw Bay, L. Huron Herring Gull #2	15	50	40	7	5	117	70	ND	08	ND	28	186	GL3
Bay Port, L. Huron Carp	5	12	5	6	1	27	27	21	ND	31	32	111	GL7
L. Huron 79-06 (Duplicate analyses) (1)	32	27.5	16.3	8.7	6.3	91							GL13
Lake Trout (2)	19	29	16	4	2	70							
Tittabawassee River-below Dow Dam Carp	37	73	145	31	4	290	81	31	44	53	14	223	GL9
L. St. Clair 79-12 Walleye	4	4.2	0.7	0.7	2.6	12							GL14
L. Erie 79-09 Walleye	17.6	9.2	5.7	5.3	2.2	40							GL15
Port Clinton, L. Erie Carp	5	5	2	4	1.5	17.5	ND	9	ND	11	30	50	GL3
Saugatuck, L. Michigan Lake Trout	35	41	8	1.4	1.4	87	5	ND	ND	ND	ND	5	GL4

TABLE 6 (Continued)

Residues of Dibenzofurans and Dibenzo-p-dioxins in Composite Samples of Fish and Gulls From Different Sites on the Great Lakes. Residues are in parts-per-trillion and by Number of Chlorine Substitutions

Site and Sample	Dibenzofurans						Dibenzo-p-Dioxins						Sample Index No.
	4Cl	5Cl	6Cl	7Cl	8Cl	Total	4Cl	5Cl	6Cl	7Cl	8Cl	Total	
L. Michigan-79-check Lake Trout	33	61	10.4	4.4	2	110							GL16
Keweenaw, L. Superior Bloater Chub	26	9	2	1	2	40	ND	ND	ND	ND	ND	ND	GL5
Isle Royale, L. Siskiwit, -L. Superior Lake Trout	10	5	ND	ND	Trace	15	ND	ND	ND	ND	Trace	Trace	GL10
L. Superior 79-02 Lake Trout	19	8.8	5.4	3.7	2.7	40							GL12
Roosevelt Beach, L.* Ontario, Brook Trout	19	4	3	3	3	32	33	ND	ND	ND	ND	33	GL6
L. Ontario 79-10 Lake Trout	34	48	29	6	2	119							GL11

at 1 and 9 ppb (7). The presence of these contaminants was suspected of causing the illnesses noted in the cattle. Analyses conducted for PCDDs, by the State of Michigan, on the PCP treated wood in barns established the link between the wood and the presence of PCDDs in the cattle samples (32). OCDD ranged from 289-5000 ppb, HpCDDs from 9-1161 ppb, and HxCDDs from non-detectable to 3.7 ppb in the wood.

K. U.S. EPA Assessment of Environmental Contamination in the Area of Hemlock Michigan (October, 1980)

As a result of numerous health complaints involving humans and domestic animals, the U.S. EPA conducted a major environmental assessment of the Hemlock, Michigan area during 1980 (33). Citizens were dissatisfied with previous studies (negative findings) conducted by county and state agencies. Residents were concerned that potable groundwater had been contaminated from a brine reinjection system operated by Dow Chemical in that area.

An extensive study of TCDD in environmental and biological samples yielded no positive results at a detection limit of low ppt levels. Downspout soils, house dusts, a well sediment sample, a septic tank sludge, and sediment samples from Dow's injection systems were also analyzed.

L. Crete Metals, Crete, Illinois (December, 1980)

TCDD and TCDF analyses were performed in 1980 on environmental and biological samples as a result of health complaints and the death of several horses near a wire reclamation facility (34). In the reclamation process, insulating and other materials were burned off wires, x-ray plates and transformer cables and other unknown metal containing products. The samples analyzed and results obtained are presented below in Table 7.

TABLE 7

	TCDD (ppt)	TCDF (ppt)
Stack #2 (Scrapping)	410	11,600
Furnace #2 (Scrapping)	58	730
Soil (on site)	21	230
Adipose (dead horse)	45	165

A variety of isomeric forms of TCDD and TCDF were detected, however, the analytical technique utilized could not adequately discriminate and quantify the isomers.

M. Dow Chemical Study of Wives of 2,4,5-T Workers (January, 1981)

No significant differences in miscarriages, stillbirths, infant deaths, or malformations were noted between wives of 2,4,5-T workers and unexposed workers (35). Other factors, such as the mother's age, complications during delivery, smoking, and mother's occupation, did not reveal any links with reproductive anomalies and exposure to 2,4,5-T. In the unexposed group, Dow reported 2031 conceptions compared to 737 in the control group, suggesting that 2,4,5-T exposure may affect fertility.

VIII. Federal Regulations on PCDDs and PCDFs

Except for disposal requirements for wastes containing 2,3,7,8-TCDD, no other regulations exist for PCDDs and PCDFs (36). Not considering carcinogenicity, the acceptable daily intake (ADI) for TCDD has been calculated at 10^{-4} µg/kg/day (37). Based upon Dow's two year study on rats, the ADI should be 10^{-5} µg/kg/day (38). At this level, a 154 pound person could only consume 1/2 pound of fish per week with 22 ppt TCDD, considerably lower than the advisory limit of 100 ppt set by the FDA. The draft ambient water quality criteria is 4.55×10^{-8} µg/l to reduce the lifetime human carcinogenic risk to 10^{-6} (14). If this criteria would be extrapolated to fish, not even one kg of fish (2.2 pounds) containing 1 ppt 2.3,7,8-TCDD could be consumed during a lifetime to keep the risk at 10^{-6} for cancer. No criteria for aquatic wildlife have been drafted.

IX. Conclusions

1. Major environmental contamination with PCDDs and PCDFs. particularly with 2,3,7,8-TCDD isomer is due to the release of commercial products containing these contaminants and secondarily from the combustion of chlorophenolic or similar compounds (i.e., PCBs).

2. Other combustion sources, such as automobiles and coal fired power plants, appear to be insignificant sources of PCDDs and PCDFs.

3. Dow Chemical of Midland, Michigan, has extensively contaminated their facility with PCDDs and PCDFs and has been the primary contributor to contamination of the Tittabawassee and Saginaw Rivers and Lake Huron.

4. The differential contamination of biological samples from the Great Lakes, being largely confined to Lake Huron and Ontario, suggests that industrial contamination is responsible.

5. The consumption of fish from the Tittabawassee River, the Saginaw River, Saginaw Bay, and possibly other sites in the Great Lakes should be prohibited.

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A REPORT ON POLYCHLORINATED DIBENZO-P-DIOXINS (PCDDs) AND POLYCHLORINATED DIBENZOFURANS (PCDFs): A SUMMARY OF STUDIES CONDUCTED IN THE GREAT LAKES AREA

U.S. ENVIRONMENTAL PROTECTION AGENCY
REGION V
CHICAGO, ILLINOIS

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I. Introduction

In the last several years, concern over the environmental and public health effects from the use of 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) and Silvex, plant herbicides, has increased. Chemical products containing 2,4,5-T have been shown to contain a highly toxic trace contaminant, 2,3,7,8-tetrachlorodibenzo-p-dioxin (2,3,7,8-TCDD), which is considered to be the most toxic of the 22 possible isomeric forms of TCDD. On February 28, 1979, an emergency suspension was imposed on certain uses of 2,4,5-T and Silvex based on extensive animal data showing that exposure to 2,4,5-T, Silvex and/or 2,3,7,8-TCDD resulted in fetotoxic, teratogenic, and carcinogenic effects and on selected epidemiological data (1,2). TCDDs and other chlorinated dioxins, technically known as polychlorinated dibenzo-p-dioxins (PCDDs) and related compounds, polychlorinated dibenzofurans (PCDFs) are found in certain commercial products. Those compounds which have a broad range of toxicities, are also receiving considerable attention. Evidence exists that PCDDs and PCDFs may be released to the environment by combustion processes. This report summarizes those studies involving PCDDs and PCDFs in the Great Lakes Area. This report does not address the physical, chemical, and toxicological properties of these compounds. Several extensive reviews on the properties of PCDDs and PCDFs are available (3,4,5,6). One of these reviews, "Long Term Hazards of Polychlorinated Dibenzodioxins and Polychlorinated Dibenzofurans," by Huff, et al is attached at the end of the report.

II. Sources of Polychlorinated dibenzo-p-dioxins (PCDDs) and dibenzofurans (PCDFs) in Commercial Products

A. 2,4,5-T and Silvex (phenoxy herbicides)

2,3,7,8-TCDD is formed in the manufacture of 2,4,5-trichlorophenol from 1,2,4,5-tetrachlorobenzene, especially if production temperatures exceed 160°C(5). Drums of Agent Orange, a mixture of 2,4,5-T and 2,4,-D, stored in the USA and in the Pacific prior to 1970 have been reported to have 2,3,7,8-TCDD levels ranging from 0.1 to 47 ppm (7). Only trace levels of other PCDDs and PCDFs were found. In 1978, producers of 2,4,5-T reported that their products contain less than 0.1 ppm of 2,3,7,8-TCDD (5).

B. Chlorinated Phenols

PCDDs and PCDFs have been found in tri, tetra, and pentachlorophenols (4,8,9). The quantities of these compounds and their isomeric forms depend upon the reaction process and conditions. In 1978 concentrations of 2,3,7,8-TCDD in 2,4,5-trichlorophenol and its sodium salt were found to be less than 0.1 ppm (10). Analyses of PCDDs in commercial grade pentachlorophenols (PCP) produced by various manufacturers during the years 1975 to 1977 found hexa-CDDs (HxCDDs) (non-detectable (N.D.) to 520 ppm), hepta-CDDs (HpCDDs) (125 to 180 ppm) and octa-CDDs (OCDDs) (N.D. to 3600 ppm). No TCDDs were found in commercial PCP. There were several isomeric forms of HxCDD, the major isomers being the 1,2,3,6,8,9; 1,2,3,6,7,8; and 1,2,4,6,7,9. The isomeric forms for HpCDD were 1,2,3,4,6,7,9 and 1,2,3,4,6,7,8(8). PCDFs were also detected in PCP including hexa-CDFs (HxCDFs) (9 to 90 ppm), HpCDFs (70 to 400 ppm) and OCDFs (55 to 260 ppm).

C. Other Chemicals

PCBs have been shown to contain 1-10 ppm of various PCDFs (11). Hexachlorophene has been reported to contain traces of TCDDs (4).

III. Sources of PCDDs and PCDFs from Pyrolysis, Photolysis and Combustion Processes

A. Chlorophenols and Related Compounds

The pyrolysis or combustion of chlorophenols, chlorophenoxy compounds or their derivatives has been shown to produce various PCDDs including TCDDs. The 2,3,7,8 isomer of TCDD has been detected in some experiments although generally as a minor component of the total TCDDs and PCDDs. Studies conducted on the burning of materials such as grass, leaves or wood chips that have been treated with chlorophenols or related compounds have also demonstrated that PCDDs are formed (7,12-16).

B. Formation of PCDFs by Pyrolysis

1. The pyrolysis of commercial PCBs (Aroclor 1254 and 1260) at temperatures of 500-600°C has been shown by Buser and his co-workers to yield 30 major and more than 30 minor PCDFs. From 3 to 25% of the pyrolyzed PCB was converted to PCDFs. Above 700°C only trace amounts of PCDFs are formed due to the complete destruction of PCB. The formation of PCDFs was shown to be the result of intermolecular cyclizations of PCB (11).

2. PCDDs and PCDFs are produced from the pyrolysis of tri, tetra, and pentachlorobenzenes in the presence of air. TCDDs have been found in pyrolysates of trichlorobenzene. However, the 2,3,7,8-TCDD isomer was present only as a minor constituent (12).

3. Recently it was reported that soot from the burning of transformer fluids containing 65% PCB and 35% chlorinated benzenes, mainly trichlorobenzene and tetrachlorobenzene, contained 3 ppm of 2,3,7,8-TCDD and 273 ppm of 2,3,7,8-TCDF (15).

C. Formation of PCDDs by Photolysis

Dechlorination of OCDD in pentachlorophenol produces tetra, penta, hexa and hepta chlorinated dioxins (8,17).

D. PCDDs and PCDFs from Combustion Sources and in Soil and Dust Samples

1. Total amounts of PCDDs and PCDFs in fly ash from a municipal incinerator in Switzerland were found to be 0.2 ppm and 0.1 ppm respectively. At an industrial heating facility, the fly ash contained 0.6 ppm PCDD and 0.2 ppm of PCDF. Only traces of the more toxic PCDDs (2,3,7,8; 1,2,3,7,8; 1,2,3,6,7,8; 1,2,3,7,8,9) were detected (7). More recent comprehensive studies have shown that PCDDs and PCDFs were present in the fly ash of 35 municipal incinerators in Europe up to 1 ppm amounts (4,14). The formation of PCDDs and PCDFs are thought to be from the combustion of wastes containing polychlorinated phenates related compounds (15,16).

2. A study released by Dow Chemical in 1978 and published in 1980 (18) reported no 2,3,7,8-TCDD (10 ppb detection level) in fly ash from their oil and coal power plant; however, 38 ppb of other TCDD isomers were found at a detection limit of 20 ppb. Detectable levels of PCDDs were found in samples from fireplaces, automobile and truck mufflers and cigarette smoke. The authors concluded that dioxins have been present since the advent of fire. The results of their study are presented in Table 1 on page 6. In contrast to the 1978 report, the authors in their 1980 article tempered their remarks by stating that some combustion sources may be sources of airborne and waterborne particulates containing PCDDs. It was theorized that the formation of PCDDs could be the result of a reaction between inorganic chloride and organic material and not due to the condensation of preexisting polychlorinated phenols. The 1980 report also included

data on emissions from a rotary kiln incinerator operated by Dow Chemical and analyses of soils and dusts collected between 1976 and 1978. Particulate matter collected from the rotary kiln incinerator, operated without natural gas and burning solid wastes from the facility, had levels of total TCDD reaching 13,200 ppb (Table 2). Two of the samples collected had levels of the 2,3,7,8-isomer greater than all other TCDD isomers. No TCDD emissions were noted when the facility was operated with natural gas. Other PCDDs were found to be substantially reduced (>95%). Analyses were also performed on particulates filtered from the scrubber water (Table 3). Levels of 2,3,7,8-TCDD and other isomers were reduced by 90% when the kiln was operated with natural gas. Results of soil and dust samples reported by the authors are presented in Table 4. The highest levels of PCDDs in soil and dust samples were those collected at the Midland plant and could be from combustion sources and/or chlorophenolic production by Dow Chemical. Evaluation of all data reported has been made by EPA personnel (19,20).

3. The results of Kimble and Gross (21) contrasted with the Dow Chemical findings. At one coal fired power plant they found no TCDD at a detection limit of 1.2 ppt in fly ash. Based upon work in their laboratory Lustenhouwer, et al, (14) have questioned the extraction method used by Kimble and Gross; however, the method was not exactly duplicated (43). In addition, the apparently negative results of Kimble and Gross have subsequently been corroborated by EPA from tests on fly ash obtained from seven coal-fired power plants (44,45).

TABLE 1

PCDDs and PCDFs
In Fly Ash and Other Combustion Sources (Reference #18)

Sample	Number of samples	Apparent dioxin content, ng/g(ppb)					
		TCDD					
		Other isomers	2,3,7,8-	Total	HCDD	HXCDD	OCDD
Incinerators, powerhouse							
• Dow powerhouse	1	38(20)	N.D.(10)	38(20)	2	4	24
• Dow rotary incinerator stack (present normal operation with supplemental fuel)	5			N.D.(2)	1-5	4-100	9,350
• Dow stationary tar burner stack (normal operation with supplemental fuel)	5	N.D.	N.D.	N.D.	1-20	27-160	130-440
• U.S. municipal incinerator (electrostatic precipitator)(Nashville, TN)	1	7.3	0.4	7.7	14	28	30
European municipal incinerators				2-20	30-200	60-130	40-120
Mufflers							
Diesel truck muffler	2	0.02	0.003	0.023	0.020	0.100	0.26
Auto muffler	4	N.D.-0.004	N.D.-0.004	N.D.-0.008	N.D.	0.003-0.01	0.02-0.07
Other sources							
Home fireplace soot	2	N.D.-0.3	N.D.-0.1	N.D.-0.4	0.2-3	0.7-16	0.9-25
Home electrostatic precipitator	1	0.4(0.4)	0.6	1.0	34	430	1,200
Cigarette smoke	2	N.D.	N.D.	N.D.	0.004-0.008	0.009	0.02-0.05
Charcoal-broiled steak	4	N.D.	N.D.	N.D.	N.D.	N.D.	0.03(0.03)

Where multiple samples were analyzed from similar sources, the range of observed values is shown. 2) N.D. indicates that the signal observed was less than 2.5 times noise. Limits of detection not within these ranges are shown parenthetically after the value reported for signals between 2.5 and 10 times noise. 3) Data without supplemental fuel is not included here because this practice has been eliminated.

TABLE 2

Chlorinated Dioxin Content of Particulate Matter

From a Rotary Kiln Incinerator

(Reference #18)

Fuel[1]			Apparent dioxins, ng/g (ppb)				
Sample	Kiln	Secondary	Other isomers TCDD	2,3,7,8-TCDD	HxCDD	H$_p$CDD	OCDD
			Without supplemental fuel				
R_1F_1	T,SW,G	T	1,800	2,800[2]	13,000	110,000	180,000
R_1F_2	T,SW,G		5,000	8,200[2]	65,000	510,000	810,000
R_2F_1	T,SW,G		3,300	110	1,300	2,000	3,000
R_3F_1	T,SW,G		12,000	N.D.(260)[3]	5,600	37,000	59,000
			With supplemental fuel				
R_3	T,SW,G	O,G	N.D.(8.0)	N.D.(2.0)	1.4	13.0	30.0
R_4	T,SW,G		N.D.(7.0)	N.D.(5.0)	N.D.(1.0)	4.0	9.0
R_5	T,SW,G		N.D.(2.0)	N.D.(2.0)	N.D.(0.5)	6.0	15.0
R_6	T,SW,G	T,G	N.D.(2.0)	N.D.(4.0)	5.0	27.0	170.0
R_7	T,SW,G		N.D.(2.0)	N.D.(2.0)	4.0	110.0	950.0

1. T, tars; SW, solid waste; G, gas; O, oil.

2. The high results reported for the 2,3,7,8-isomer are probably due to analysis by the nonspecific GC-MS packed-column method. Later results were obtained with a capillary column specific for 2,3,7,8-TCDD. The TCDD results from run 1 (R_1) are not comparable to those from runs 2 and 3.

3. Numbers in parentheses are limits of detection.

TABLE 3

Chlorinated Dioxins in Rotary Kiln Incinerator Scrubber Water

(Reference #18)

Sample	Apparent dioxins, ng/g (ppb)				
	Other isomers TCDD	2,3,7,8-TCDD	HxCDD	H_pCDD	OCDD
Particulates filtered from scrubber water					
Without supplemental fuel	300	2,200 *	3,400	26,000	42,000
With supplemental fuel	14	32*	200	970	1,200
Filtered scrubber water without supplemental fuel	0.0018(0.01)**	0.001*(0.0006)**	0.005	0.024	0.026

* The analytical method did not separate 2,3,7,8-TCDD from 11 other isomers.

** Numbers in parenthesis are limits of detection.

TABLE 4

Chlorinated Dioxins in Soils and Dusts (Reference #18):

	Number of samples	Apparent dioxin content, ng/g (ppb)[1]					
		Other isomers TCDD	2,3,7,8-TCDD	Total TCDD	HxCDD	HpCDD	OCDD
Soil							
Rural (Gaylord, MI)	5			N.D.[2]	N.D.	N.D.-0.05	N.D.-0.2
Urban (Lansing & East Lansing, MI)	5			N.D.	0.03-1.2	0.03-2	0.05-2
Major metropolitan (Chicago, IL)	8			0.005-0.03	0.03-0.3	0.1-3	0.4-22
Dow Chemical (Midland, MI)	5	0.8-18	0.3-100	1-120	7-280	70-3,200	490-20,0
Dust							
Dow Chemical lab.	6	0.5-2	0.7-3	1-4	9-35	140-1,200	650-7,50
Midland, Michigan	2			0.03-0.04(0.02)[3]	0.2-0.4	2-4	20-30
Metropolitan (Detroit, MI)	4			N.D.-(0.03)	N.D.-0.3	0.3-4	0.1-4
Metropolitan (St. Louis, MO)	1	0.16	0.12	0.3	2	34	210
Metropolitan (Chicago, IL)	2			0.04(0.04)	N.D.-0.3	0.6-3	3-8

1. Where multiple samples were analyzed from similar sources, the range of observed values is shown.
2. N.D. = Not Detectable
3. Value in parentheses indicates detection limit.

IV. Studies Involving PCDDs and PCDFs Conducted in the Great Lakes Area

A. Dow Chemical Monitoring Study, Midland, Michigan (June, 1978)

In June, 1978, Dow Chemical reported results of their monitoring program to the Michigan Department of Natural Resources (MDNR) as requested by that agency (22). The data has been summarized below.

1. Tittabawassee River Water and Sediment (1976)

Ten samples (two water and eight sediment) from the Tittabawassee River and below the plant showed no detectable amounts of TCDDs. The detection limit (DL) for sediments ranged from 10 to 50 ppt. Water samples were analyzed at a DL of 1 ppt.

2. Plant Discharge Stream (1976-1978)

Composite and grab samples of wastewater discharge revealed no detectable levels of TCDDs in 13 of 14 samples (DL=5 ppt or less). One sample was found to contain 8 ppt of TCDDs.

3. Bioconcentration Study (1978)

Analyses performed on the edible portions of fish flesh from caged trout placed six miles downstream of the plant's effluent for periods of 7,14, and 30 days revealed no detectable level of TCDDs at a DL of 10 to 30 ppt. Five of six fish placed in the tertiary effluent stream for 7 days were found to have TCDDs ranging from 20 to 50 ppt at a DL of 10 to 20 ppt. When analyses were also performed on whole fish, the 30 day trout (downstream) showed TCDDs ranging from 10 to 20 ppt when analyzed at a DL of 5 ppt. The fish collected from the tertiary effluent stream showed higher levels of TCDDs ranging from 50 to 70 ppt at a DL of 20 ppt. Analyses on the 7 day trout (edible and whole fish) caged along the river bottom revealed no TCDDs at a DL of 10 to 40 ppt. No TCDDs were detected in analyses performed on the edible portions of fish flesh from unexposed control fish (DL=20 ppt) and those placed in the river at Dow dam (DL=20 ppt), indicating that TCDDs could be present in the plant's effluent (4).

4. Native Fish Studies

(a) 1976 (Analyses 1978)

TCDDs were detected in 4 of 9 catfish samples, edible portions, at levels ranging from 70 to 230 ppt. Three of the four samples in which TCDDs were detected were located downstream of the plant's effluent. OCDDs were found in 8 of 9 fish, collected both upstream and downstream of the discharge. The levels ranged from 40 to 150 ppt. One fish sample was positive for HxCDDs (90 ppt). Detection limits ranged from 10 to 200 ppt.

(b) 1977 (Analyses 1978)

Fish caught downstream of Dow at Smith's Crossing (Figure 1) in the Tittabawassee River revealed contamination in 9 of 14 fish tested. Analyses were performed on the edible portions of fish flesh. The levels of TCDDs ranged from 20 to 244 ppt.

(c) Saginaw Bay 1978

Of three fish collected from Saginaw Bay, one catfish was found to contain 24 ppt TCDDs, at a DL of 10 ppt. The analyses were performed on the edible portions of fish flesh.

5. Chlorophenols

Chlorophenols were found in the Dow effluent up to levels of 70 ppb. 2,3,4,6-tetrachlorophenol and pentachlorophenol were present at ppb levels below the dam in sediments of the Tittabawassee River. Chlorophenols were also found in some fish at ppb levels above the discharge point of the plant's wastewater effluent.

Based upon these findings, the Michigan Department of Public Health issued an advisory on June 28, 1978 against consuming fish caught in the waters of the Tittabawassee and Saginaw Rivers. This health advisory is still in effect at this date (23).

B. Dow Chemical Monitoring Study, Midland, Michigan (October, 1978)

Results of PCDD sampling indicated the presence of 2,3,7,8-TCDD in 2,4,5-T sludge at 10 ppt and in trichlorophenol scrubber fluid at 20 ppt (24). The 2,4,5-T sludge also contained 11 ppt HxCDDs, 4 ppt HpCDDs, and 43 ppt OCDDs Brine wastes and sludges from 2,4-D processes were negative for PCDDs.

C. U.S. EPA TCDD Fish Monitoring Program (December, 1978)

In response to Dow's first monitoring report, which indicated incidental contamination of fish from the lower Tittabawassee River, fish were collected and analyzed from the Tittabawassee, Grand and Saginaw Rivers (25). In 26 out of 35 skinless fillet fish samples, detectable levels of 2,3,7,8-TCDD were found and ranged from 4 to 695 ppt. Eleven of these fish samples contained TCDD levels greater than 40 ppt. All but two of these samples were from locations downstream of Midland. Four out of 6 samples collected upstream were found to be negative for 2,3,7,8-TCDD. Data is presented in Table 2 on pages 14 and 15. Analyses of spiked blind controls, which consisted of various known levels of 2,3,7,8-TCDD, indicated that the positive results were within ± 20% of the values reported. Responding to a request from the Governor of Michigan, the FDA recommended that fish containing TCDD (2,3,7,8-TCDD) at a level of more than 100 ppt not be consumed. Where 2,3,7,8-TCDD had been found in fish below 100 ppt, it was recommended that no more than one average size portion of fish be consumed per week (26).

D. U.S. EPA-Michigan Monitoring Study of Dow Chemical, Midland, Michigan (April, 1979)

Results of TCDD analysis of samples taken from Dow's 2,4,5-Trichlorophenol injection well (DL=0.06 ppt), phenol treatment system (DL=82 ppt), plant effluent (DL=0.002 ppt) and upstream Tittabawassee River (DL=5.0 x 10^{-5} ppt), were found to be negative. However, the carbon filter concentration system utilized was believed to be unsuitable for concentrating contaminants found in water (27).

E. Dow Chemical Study on Fish, April 1979

As part of Dow's study on dioxin the company reported finding the following ranges of dioxins in parts per trillion (ppt) in fish collected from other tributaries of the Saginaw River (28).

	Number of Samples	Number of Positive Results	TCDDs	HxCDDs	HpCDDs	OCDDs
Flint Fiver	6	5	ND-11	ND-6	ND-5	ND-20
Cass River	6	4	ND-104	ND-11	ND-11	ND-44
Shiawasse River	6	1	ND-9	ND	ND	ND

ND=not detected

F. Composite Fish Sample from the Tittabawassee River (December 1980)

A single composite whole fish sample of five carp, supplied by the MDNR, (collected downstream of Midland) and analyzed by Columbia National Pesticide Laboratories, yielded positive results for various PCDDs and PCDFs (29). The 2,3,7,8-isomer of TCDD constituted >90% of the TCDDs found (30,31). The results are shown below:

	TCDDs	81		TCDFs	37
	PCDDs	31		PCDFs	73
	HxCDDs	44		HxCDFs	145
	HpCDDs	53		HpCDFs	31
	OCDDs	14		OCDFs	4
Total	PCDDs	223 ppt	Total	PCDFs	290 ppt

TABLE 5

RESULTS OF 2,3,7,8-TETRACHLORODIBENZO-P-DIOXIN (TCDD) FISH MONITORING PROGRAM CONDUCTED BY THE U.S. ENVIRONMENTAL PROTECTION AGENCY IN MICHIGAN DURING 1978

LOCATION	FISH SPECIES	FISH LENGTH (cm)	* TCDD LEVEL (ppt)a	TCDD DETECTION LIMITS (ppt)
Tittabawassee River				
Tittabawassee Road	Carp	42.2	52	8
	Yellow Perch	16.2 11.0[b]	20	8
	Carp	39.7	93	6
Freeland Road	Carp	40.0	32	4
	Yellow Perch	16.8 12.3	10	5
Smith's Crossing Road	Channel Catfish	50.3	273	6
	Carp	38.0	22	11
	Channel Catfish	38.2	695	60
	Carp	23.1	49	1
	Sucker	35.6	8	4
	Sucker	38.1	21	4
Above Dow Dam	Channel Catfish	30.9	42	9
	Carp	34.6	ND[c]	5
	Carp	33.0	ND	9
	Channel Catfish	38.1	28	2
	Yellow Perch	19.3	ND	4
Dublin Road	Carp	52.2	ND	9

* Skinless Fillets

TABLE 5 (cont'd)

LOCATION	FISH SPECIES	FISH LENGTH (cm)	* TCDD LEVEL (ppt)a	TCDD DETECTION LIMITS (ppt)
Saginaw River				
Wickes Park	Carp	46.0	62	13
	Yellow Perch	11.9 11.4	ND	11
Block's Marina	Channel Catfish	69.0	105	7
	Channel Catfish	48.5	52	8
	Carp	51.8	28	4
Mouth	Channel Catfish	46.0	30	6
	Carp	45.0	153	13
	Yellow Perch	16.0 16.0	11	4
Grand River				
Jones Road near Eagle	Carp	39.0	20	4
	Carp	39.0	41	8
	Channel Catfish	----	29	6
	Smallmouth Bass	35	7	6
	Smallmouth Bass	38.0	8	6
Near Ionia	Carp	50.8	ND	2
	Sucker	48.3	ND	2
Saginaw Bay				
Lat. 43 40' 16"	Sucker	28.2 31.0	4	2
Long. 83 50' 21"	Yellow Perch	24.2 26.8	ND	3

* Skinless Fillets

TABLE 5 (cont'd)

Location	FISH SPECIES	FISH LENGTH (cm)	* TCDD LEVEL (ppt)[a]	TCDD DECTECTION LIMITS (ppt)
Lake Michigan				
Off Saugatuck	Lake Trout	50.8	ND	7

---

a ppt indicates parts per trillion which is equivalent to ng/kg.

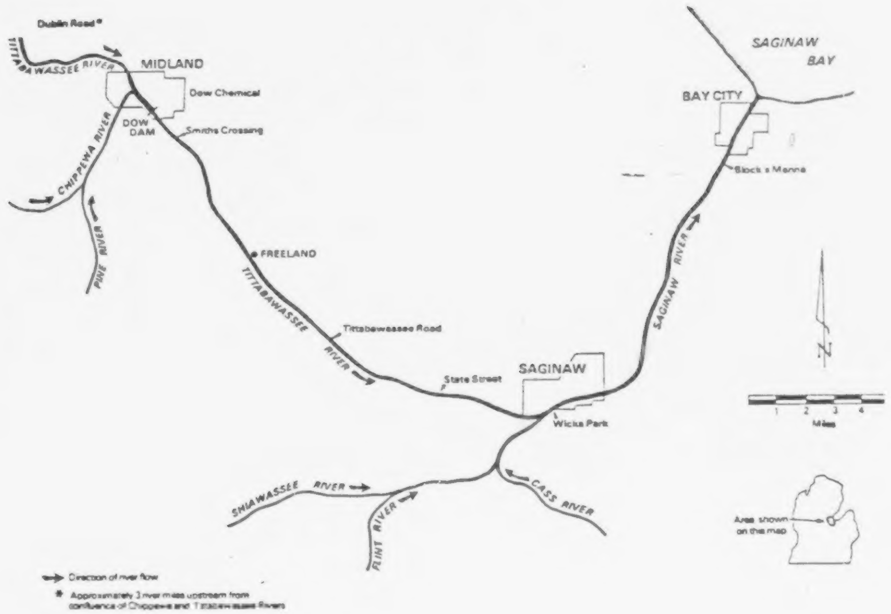
b signifies composite fish sample.

c ND indicates that TCDD was not detected in the fish sample at the corresponding detection limit.

* Skinless Fillets

FIGURE 1:

SAGINAW RIVER BASIN


Dublin Road*
TITTABAWASSEE RIVER
MIDLAND
Dow Chemical
CHIPPEWA RIVER
DOW DAM
Smiths Crossing
PINE RIVER
FREELAND
TITTABAWASSEE RIVER
Tittabawassee Road
State Street
SAGINAW
Wicks Park
SAGINAW BAY
BAY CITY
Block's Marina
SAGINAW RIVER
N
1
2
3
4
Miles
SHIAWASSEE RIVER
FLINT RIVER
CASS RIVER
Area shown on the map
Direction of river flow
* Approximately 3 river miles upstream from confluence of Chippewa and Tittabawassee Rivers

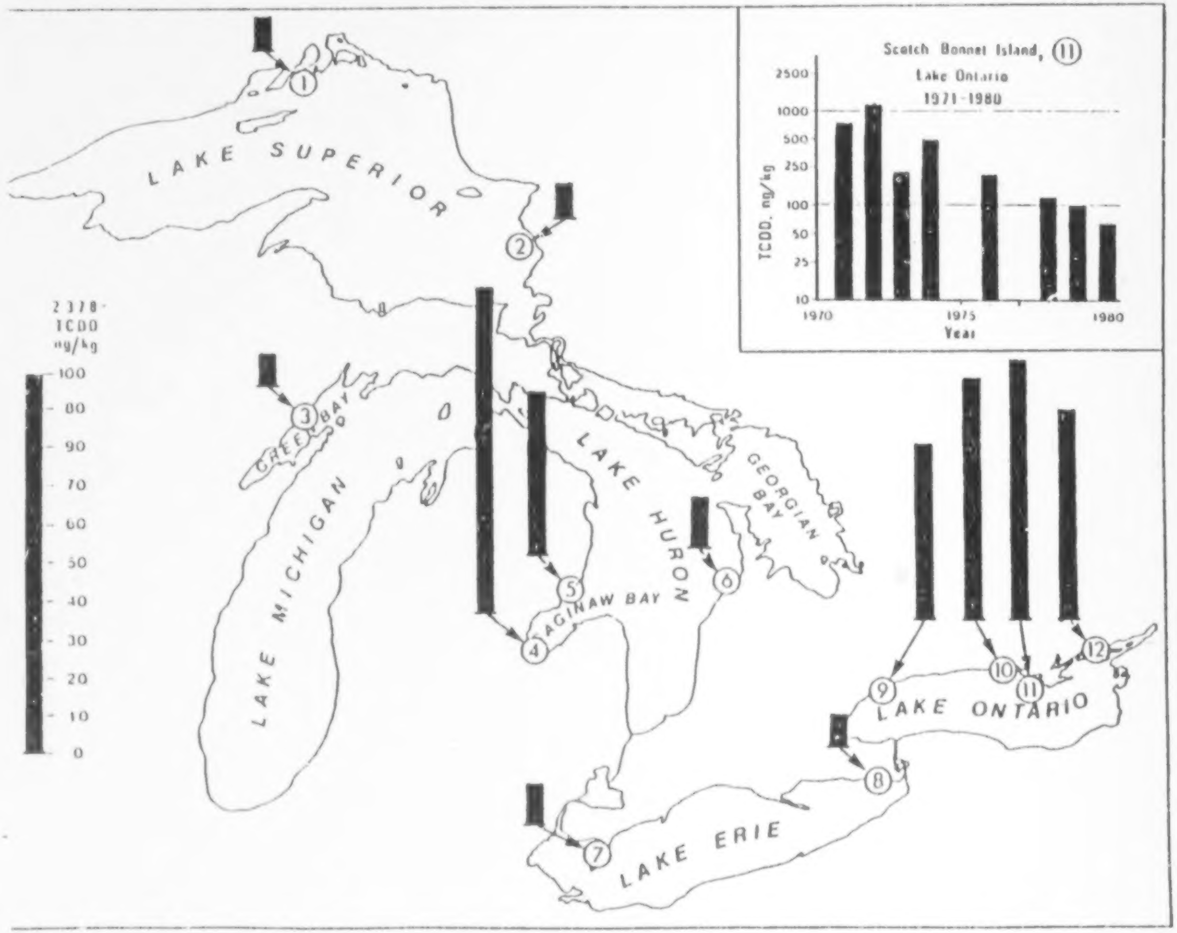
G. Canadian Study on Gull Eggs from the Great Lakes

Dr. Douglass Hallet of the Canadian Wildlife Service reported finding 2,3,7,8-TCDD in Herring gull eggs, collected in 1980, at 12 different locations within the Great Lakes (32). The highest levels of 2,3,7,8-TCDD were found in Saginaw Bay eggs (43-90 ppt). Levels in Lake Ontario eggs were slightly lower and ranged from 44-64 ppt. Lower levels (approximately 3-10 ppt) were found in eggs collected at other Great Lakes sites. The 2,3,7,8-TCDD isomer was found to predominate (>90%). These results are graphically presented in Figure 2. There have been no reports of abnormalities in gull chicks or mature birds. Egg samples collected from Lake Ontario in 1971 and preserved until analysis in 1980 had 2,3,7,8-TCDD levels of 800 ppt. It was conjectured that the decrease in 2,3,7,8-TCDD levels since 1971 (Figure 2) might be attributed to the discontinuation of 2,4,5-trichlorophenol production by Hooker Chemical at Niagara Falls, New York in 1971. Confirmational analyses of gull egg samples are now underway in U.S. laboratories.

H. Gull Flesh Analyses From the Great Lakes (December 1980)

Two flesh samples from gulls in the Saginaw Bay were recently analyzed by Dr. David Stalling of the Columbia National Fisheries Research Laboratory (30). In the two samples, the 2,3,7,8-TCDD isomer predominated (>90%) and was found at levels of 70 and 160 ppt (31). HxCDDs and OCDDs were also found resulting in a total PCDD level of 186 and 196 ppt. Total PCDFs were found at 117 and 121 ppt with the PnCDFs and HxCDFs being the predominate furans.

Figure 2: "Dioxin in Gull Eggs" (Reference 27)


Scotch Bonnet Island, ⑪
Lake Ontario
1971-1980
2500
1000
500
250
100
50
25
10
TCDD, ng/kg
1970
1975
1980
Year
2378-
TCDD
ng/kg
100
80
90
70
60
50
40
30
20
10
0
LAKE SUPERIOR
LAKE MICHIGAN
GREEN BAY
LAKE HURON
SAGINAW BAY
GEORGIAN BAY
LAKE ERIE
LAKE ONTARIO
①
②
③
④
⑤
⑥
⑦
⑧
⑨
⑩
⑪
⑫

I. PCDD and PCDF Analyses on Great Lakes Fish (April 1981)

1. The Columbia National Fisheries Research Laboratory has obtained positive results for TCDDs and TCDFs on composite whole fish samples from the Great Lakes (29). This fish sampling is being conducted under the National Pesticides Monitoring Program. Huron and Ontario fish samples ranged in TCDD concentrations from 33 to 94 ppt. The highest values were reported in fish collected from Saginaw Bay in 1978. Data collected to date is presented in Table 6. Tittabawassee fish data (see E. above) is included for comparison. The predominate (>90%) isomeric form of TCDD discovered has been 2,3,7,8-TCDD (30,31). The majority (>90%) of the other chlorinated dioxins and furans found in fish appear to have the 2,3,7,8 ring positions chlorinated (30,31). Therefore, the potential toxicity of these dioxins and furans may approach that of 2,3,7,8-TCDD (3). Very preliminary data indicates that the isomeric distribution of PCDDs and PCDFs in river sediments do not reflect those found in fish (31,33). Differences in solubilities of PCDDs and PCDFs, absorption or retention of these chemicals could account for the observed difference in distribution (33).

2. The FDA has also reported finding TCDDs in fish from Saginaw Bay. Analyses performed by FDA on edible fillets from 27 fish collected from Saginaw Bay in 1979, determined four to be positive for TCDDs (21 to 45 ppt). FDA recommended that fish having TCDD residues above 100 ppt should not be consumed and even lower levels, down to 50 ppt, consumption should be limited. FDA stated that no adverse health consequences would be anticipated from the moderate consumption of fish containing TCDD residues below 50 ppt (34).

TABLE 6

Residues of Dibenzofurans and Dibenzo-p-dioxins in Composite Samples of Fish and Gulls From Different Sites on the Great Lakes. Residues are in parts-per-trillion and by Number of Chlorine Substitutions (29).

Site and Sample	Dibenzofurans						Dibenzo-p-Dioxins						Sample Index No.
	4Cl	5Cl	6Cl	7Cl	8Cl	Total	4Cl	5Cl	6Cl	7Cl	8Cl	Total	
Saginaw Bay, L. Huron Carp	27	44	34	44	4	153	94	157	122	12	ND	305	GL1
Saginaw Bay, L. Huron Herring Gull #1	16	28	57	17	3	121	160	ND	20	ND	19	199	GL2
Saginaw Bay, L. Huron Herring Gull #2	15	50	40	7	5	117	70	ND	88	ND	28	186	GL3
Bay Port, L. Huron Carp	5	12	5	6	1	27	27	21	ND	31	32	111	GL7
L. Huron 79-06 (Duplicate analyses) Lake Trout (1)	32	27.5	16.3	8.7	6.3	91							GL13
(2)	19	29	16	4	2	70							
Tittabawassee River-below Dow Dam Carp	37	73	145	31	4	290	81	31	44	53	14	223	GL9
L. St. Clair 79-12 Walleye	4	4.2	0.7	0.7	2.6	12							GL14
L. Erie 79-09 Walleye	17.6	9.2	5.7	5.3	2.2	40							GL15
Port Clinton, L. Erie Carp	5	5	2	4	1.5	17.5	ND	9	ND	11	30	50	GL8
Saugatuck, L. Michigan Lake Trout	35	41	8	1.4	1.4	87	5	ND	ND	ND	ND	5	GL4

TABLE 6 (Continued)

Residues of Dibenzofurans and Dibenzo-p-dioxins in Composite Samples of Fish and Gulls From Different Sites on the Great Lakes. Residues are in parts-per-trillion and by Number of Chlorine Substitutions (29).

Site and Sample	Dibenzofurans 4Cl	5Cl	6Cl	7Cl	8Cl	Total	Dibenzo-p-Dioxins 4Cl	5Cl	6Cl	7Cl	8Cl	Total	Sample Index No.
L. Michigan-79-check Lake Trout	33	61	10.4	4.4	2	110							GL16
Keweenaw, L. Superior Bloater Chub	26	9	2	1	2	40	ND	ND	ND	ND	ND	ND	GL5
Isle Royale, L. Siskiwit, L. Superior Lake Trout	10	5	ND	ND	Trace	15	ND	ND	ND	ND	Trace	Trace	GL10
L. Superior 79-02 Lake Trout	19	8.8	5.4	3.7	2.7	40							GL12
Roosevelt Beach, L. Ontario, Brook Trout	19	4	3	3	3	32	33	ND	ND	ND	ND	33	GL6
L. Ontario 79-10 Lake Trout	34	48	29	6	2	119							GL11

3. The New York State Department of Health is currently screening Lake Ontario fish for contamination. Previous analyses conducted on two fish determined dioxin contamination at 4.6 and 6.5 ppt (35). A potential source of contamination may be from landfills in the Niagara River area where 2,4,5-trichlorophenol wastes were dumped (36). Sediment samples from streams which drain into the Niagara River have been reported to contain dioxin (37).

J. NIEHS Analyses of a Michigan Dairy Herd Tissue Samples and Michigan's Study on Pentachlorophenol Treated Wood (1978-1979)

Studies by NIEHS of a dairy herd in Michigan, presumed to be contaminated by contact with PCP treated wood, revealed fat and liver contamination, respectively, with OCDDs at 7 and 15 ppb; HpCDDs at 6 and 15 ppb; and HxCDDs at 1 and 9 ppb (6). The presence of these contaminants was suspected of causing the illnesses noted in the cattle. Analyses conducted for PCDDs, by the State of Michigan, on the PCP treated wood in barns established the link between the wood and the presence of PCDDs in the cattle samples (38). OCDDs ranged from 289-5000 ppb, HpCDDs from 9-1161 ppb, and HxCDDs from non-detectable to 3.7 ppb in the wood.

K. U.S. EPA Assessment of Environmental Contamination in the Area of Hemlock Michigan (October, 1980)

As a result of numerous health complaints involving humans and domestic animals, the U.S. EPA conducted an environmental assessment in 1980 of the Hemlock, Michigan area, located 14 miles south of Midland (39). Citizens were dissatisfied with previous health and environmental studies (negative findings) conducted by county and state agencies. Residents were concerned that potable groundwater had been contaminated from a brine reinjection system operated by Dow Chemical in that area. A study of TCDDs in 40 environmental and biological samples yielded only one positive result at a detection limit of low ppt levels. Several fish, downspout soils, house dusts, a well sediment sample, a septic tank sludge, and sediment samples from Dow's injection systems were found to be negative for TCDDs at detection levels ranging from 1–43 ppt (40). The one positive sample was a caged fish collected from the Tittabawassee River, downstream of Midland, which contained 23 ppt TCDDs.

L. Crete Metals, Crete, Illinois (December, 1980)

TCDDs and TCDFs analyses were performed in 1980 on environmental and biological samples as a result of health complaints and the death of several horses near a wire reclamation facility (41). In the reclamation process, insulating and other materials were burned off wires, x-ray plates and transformer cables and other unknown metal containing products.

Samples analyzed and results obtained are presented below in Table 7.

TABLE 7

	TCDDs (ppt)	TCDFs (ppt)
Stack #2 (Scrapping)	410	11,600
Furnace #2 (Scrapping)	58	730
Soil (on site)	21	230
Adipose (dead horse)	45	165

A variety of isomeric forms of TCDDs and TCDFs were detected, however, the analytical technique utilized could not adequately discriminate and quantify the isomers.

V. Current Government Activity

Except for disposal requirements for chlorophenolic wastes containing 2,3,7,8-TCDD, no other regulations exist for controlling PCDDs and PCDFs release to the environment (42). The implications of these data on the consumption of dioxin contaminated fish are currently undergoing review by various government agencies in this country and Canada.

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Long-Term Hazards of Polychlorinated Dibenzodioxins and Polychlorinated Dibenzofurans[*]

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During January 10–11, 1978 in Lyon, France, a joint National Institute of Environmental Health Sciences/International Agency for Research on Cancer ad hoc Working Group considered and discussed the feasibility of coordinating epidemiological studies on the long-term hazards associated with the chlorinated dibenzo-*p*-dioxins and chlorinated dibenzofurans (PCDDs and PCDFs). Nineteen invited scientists from eight countries presented introductory working papers summarizing the most up-to-date and relevant information available from their individual programs. This report represents the collective views and scientific opinions of the Working Group. The greater part of this document comprises epidemiological studies related to episodes of human exposure. The review begins with a brief section concerning possible routes of human exposure, an overview of the pertinent chemical characteristics, and the salient toxicological properties of the structurally similar PCDDs/PCDFs. The Working Group report ends with recommendations for future activities.

Introduction

Human exposure in the workplace can occur when chlorinated dibenzo-*p*-dioxins (PCDDs) are formed during the production of certain compounds such as the herbicide 2,4,5-trichlorophenoxyacetic acid (2,4,5-T), the fungicide pentachlorophenol, and the germicide hexachlorophene (*1*). The dioxins, impurities/contaminants associated with these end-products, result most often from treatment of chlorinated benzenes at elevated temperature and pressure under alkaline conditions. Via the widespread use of these commercial products (*1*, *2*) the general population may also become exposed.

In recent years, out-of-control chemical reactions during the production of 2,4,5-trichlorophenol have proceeded to the explosive stage thereby exposing persons to toxic levels of PCDDs. From certain of these accidents, moreover, not only did those occupationally involved receive dangerous exposure but also those inhabiting the surrounding areas received uncommon risk.

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The structurally-related chlorinated dibenzofurans (PCDFs) are contaminants found in some polychlorinated biphenyl compounds: Aroclor, Clophen, Phenoclor (*3*).

These impurities are more toxic and represent a greater environmental hazard than the compounds they contaminate (*1, 3-9*). For instance, 2,3,7,8-tetra-CDD has been recently found in beef fat from cattle grazed on 2,4,5-T-treated rangeland and in breast milk from women living in areas where 2,4,5-T is used on rangeland or in forest areas (*10*). Various investigators (*11-14*) have also discovered PCDDs and PCDFs in fly ash and flue gas from municipal incinerators, and in dust from fungicide-treated wood (*15*).

Chemical Aspects

The PCDDs and PCDFs are two series of tricyclic aromatic compounds which exhibit similar chemical and physical properties (*1, 3, 4*). The basic two-dimensional structures (I, II) have eight possible points of chemical addition. From the monochloro to the octachloro derivatives, a variety of positional isomers are possible: 75 PCDDs and 135 PCDFs (Table 1).

The extreme toxic potency of some of these compounds, as well as the large number of potential isomers, warrant analytical methods exhibiting high sensitivity and specificity to monitor the environment. A desirable detection limit of one part per trillion (ppt, 1 picogram/gram sample) is being reached with current methodology. Essential requirements included efficient clean-up, good separation and selectivity, ultrasensitive quantification, and validation (*16, 17*).

Toxicological Aspects

Animals

The prototype and most extensively studied isomer of the PCDDs and PCDFs is the 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (2,3,7,8-tetra-CDD), perhaps the most potent man-made toxin presently known. The comparative oral lethal dose values for various PCDDs in mice and guinea pigs (Table 2) show clearly that the 2,3,7,8-tetra-CDD and the 1,2,3,7,8-penta-CDD isomers are the most toxic (*18*).

Toxic effects induced by PCDDs and PCDFs vary quantitatively and quantitatively among different species; however, within a single species the untoward consequences are markedly similar for all PCDDs and PCDFs that have been studied. For example, the toxic effects induced by 2,3,7,8-tetra-CDD which are most often observed in mice, guinea-pigs, and monkeys, are illustrated in Table 3 (*20*). In a brief report, daily oral intake (12-61 days) of <1 μg/kg body weight 2,3,7,8-tetra-CDD was stated as being lethal to young male rhesus monkeys (*21*), whereas McConnell et al. (*22*) reported an LD_{50} in female rhesus monkeys as <70 μg/kg body weight.

A preliminary report on 2,3,7,8-tetra-CDF concerning the toxicity of PCDFs (*23*), and a report on PCDFs (*24*) have been published.

The toxic syndrome produced by PCDDs and PCDFs may be divided into seven categories:

Chloracne. 2,3,7,8-Tetra-CDD and the tri-PCDF and tetra-PCDF were found to be active skin irritants and to induce acneform lesions in the skin of rabbit ears (*25*).

Classical chloracne is a hallmark of PCDD exposure in humans and an analogous hyperkeratosis and the modulation of sebaceous structures to keratin cysts have been observed in monkeys, rabbits, and hairless mice.

Chloracne or acneform dermatitis is a common occupational dermatitis characterized by comedones, keratin cysts, pustules, papules, and abscesses. In 1957, Kimmig and Schulz (*26*) found that 2,3,7,8-tetra-CDD was the agent responsible for causing occupational chloracne in employees of chlorophenol-producing factories. Further, in 1971 PCDDs were implicated as causing chloracne in male workers in a plant producing 2,4-D and 2,4,5-T (*27, 28*). Chloracne may appear weeks or months after the initial exposure to PCDDs and PCDFs.

Hepatoxicity. The degree of hepatic involvement appears to be dose-dependent, and the severity of the changes produced varies between species (*29*). Hepatic necrosis produced by 2,3,7,8-tetra-CDD is probably a contributing cause of death in rats and rabbits, while hepatic necrosis and liver insufficiency are less extensive in mice and are minimal in comparison in guinea pigs and monkeys (*22, 30-37*). Hepatic porphyrin accumulation has been observed in mice, rats, and chickens.

Hypoplasia of the Lymphoid Tissues. Particularly involved are the cortical cells of the thymus and this hypoplasia has been observed in mice, rats, guinea-pigs, and monkeys. The most significant findings in both mice and guinea-pigs treated with sublethal doses of 2,3,7,8-tetra-CDD were in the lymphoid system, resulting in suppression of cell-mediated immunity, particularly in young animals (*36, 38*). Low levels of 2,3,7,8-tetra-CDD that did not produce overt clinical or pathological changes still reduced host defences: 1 μg/kg bw given orally once weekly for 4 weeks to mice before infection with Salmonella increased mortality and decreased the time from infection to death (*39*). The increased mortality may be caused by the endotoxin content of these gram negative bacteria, since 2,3,7,8-tetra-CDD markedly increases the susceptibility of mice to endotoxin (lipopolysaccharide of *Escherichia coli*) (*40*). Treatment of female mice and rats with 2,3,7,8-tetra-CDD during the latter half of gestation and in the postnatal period resulted in a severe depletion of lymphocytes in the thymic cortex of the offspring (*41*). Cellular immunity was impaired.

Hematological changes in mice, rats, and guinea pigs treated with 2,3,7,8-tetra-CDD include lymphopenia and thrombocytopenia (*42, 43*); manifest also is an increased susceptibility to infection concomitant with the suppression of cell-mediated immunity. For 9 months, female rhesus monkeys received a diet containing 500 ppt 2,3,7,8-tetra-CDD; within 6 months, the monkeys became anemic and after 9 months pancytopenic (*44*). The marked thrombocytopenia was associated with widespread hemorrhage. Death occurred in five of the eight monkeys between months 7 and 12 of the experiment at total exposure levels of 2,3,7,8-tetra-CDD of 2-3 μg/kg body weight. At autopsy, in addition to extensive hemorrhage, there was a distinct hypocellularity of the bone marrow and lymph nodes. Hypertrophy, hyperplasia, and metaplasia of the epithelium in the bronchial tree, bile ducts, pancreatic ducts, salivary-gland ducts, and palpebral conjunctivae were observed. Squamous metaplasia and keratinization of the sebaceous glands and hair follicles were present in the skin. Death was attributed to complications from the severe pancytopenia (*44*).

Table 1. Possible number of isomers for polychlorinated dibenzo-*p*-dioxins and polychlorinated dibenzofurans.

Chlorine atoms	PCDD isomers[a]	PCDF isomers[b]
1	2	4
2	10	16
3	14	28
4	22	38
5	14	28
6	10	16
7	2	4
8	1	1
Total	75	135

[a] Chlorinated dibenzo-dioxins: empirical formula $C_{12}H_{7-0}Cl_{1-8}O_2$; molecular weight ranges, 218–460.

[b] Chlorinated dibenzofurans: empirical formula, $C_{12}H_{7-0}Cl_{1-8}O$; molecular weight ranges, 202–444.

General Debilitation and Wasting. Animals that receive a toxic or lethal dose of PCDDs or PCDFs exhibit a chronic and progressive weight loss with parallel mobilization of peripheral fat, increased serum triglyceride levels, and development of a fatty liver. Death due to PCDDs or PCDFs intoxication is delayed, as exemplified by an elapsed time period of 6 to 8 weeks following administration of a lethal dose and eventual death (*18, 22, 44*).

Embryotoxicity and Teratogenicity of 2,3,7,8-tetra-CDD. In repeated or single doses of 2,3,7,8-tetra-CDD to mice, as little as 1-10 μg/kg cause increased frequencies of cleft palate and kidney abnormalities (*45-48*) (see Table 4). In rats, embryo-lethal effects occur under experimental conditions (*49, 50*), and kidney anomalies (*45*), intestinal hemorrhages, and general edema can be produced in the fetuses (*51*). Few follow-up studies of the effects of prenatal exposure on postnatal functions have been published. In mice, fetal kidney abnormalities caused by 2,3,7,8-tetra-CDD may progress into a hydronephrosis during the postnatal period (*52*).

Chick Edema Disease. Hydropericardium, ascites, subcutaneous edema, liver necrosis, and death were described in 1957 following the accidental administration of toxic fats in the feed of broiler chickens (ascites have been observed also in mice) (*1*). The toxic material was later identi-

Table 2. Estimated single oral LD50-30 values of certain polychlorinated dibenzo-p-dioxin isomers.[a]

Chlorine isomer	Guinea pigs		Mice	
	μg/kg	μmole/kg	μg/kg	μmole/kg
2,8	>300,000	>1,180	—	—
2,3,7	29,444	120.41	>3,000	>10
2,3,7,8	2	0.006	283.7	0.88
1,2,3,7,8	3.1	0.009	337.5	0.94
1,2,4,7,8	1,125	3.15	>6,000	>14
1,2,3,4,7,8	72.5	0.185	825	2.11
1,2,3,6,7,8	70–100[b]	0.178–0.255	1,250	3.19
1,2,3,7,8,9	60–100[b]	0.153–0.255	>1,440	>3.67
1,2,3,4,6,7,8	>600	>1,400	—	—
1-NO_2-3,7,8	>30,000	>90	—	—
1-NH_2-3,7,8	>30,000	>99	—	—
1-NO_2-2,3,7,8	47.5	0.129	>2,000	>5.4
1-NH_2-2,3,7,8	194.2	0.576	>4,800	>14.2

[a] Data from McConnell et al. (18). The LD_{50-30} was calculated by the Spearman-Karber method (19).

[b] Estimated range due to variability in replicates.

fied in commercial oleic and stearic acids produced from inedible tallow recovered from animal hides; trichlorophenols and pentachlorophenols had been used in the curing of the hides. The edema causative was termed toxic fat and more specifically chick edema factor and was characterized by x-ray crystallography as 1,2,3,7,8,9-hexa-CDD (53). 2,3,7,8-Tetra-CDD, hexa-CDD, and octa-CDD have been also identified in several commercial fatty acids (54). Daily doses of 10 or 100 μg hexa-CDD/kg bw, or of 1 or 10 μg 2,3,7,8-tetra-CDD/kg bw, produced a positive response in the chick edema bioassay; 0.5% octa-CDD in the diet had no effect (35). Similar edematous effects were observed in rats, pigs, dogs, and monkeys, but not in guinea pigs (55). Decreased serum albumin may be associated with the edema; edema has been also shown to occur in chicks dosed orally with 2,3,7,8-tetra-CDF (56).

Table 3. Summary of the toxic effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin.[a]

	Mice	Guinea pigs	Monkeys (female)
Thymus involution	+++	+++	+++
Spleen reduction (white pulp)	+	+	+
Bone marrow hypoplasia	±	++	+
Liver megalocytosis/generation	+++	−	−
Bile duct hyperplasia	±	±	+++
Testicular degeneration	++	+++	NA
Renal pelvis hyperplasia	−	++	+
Urinary bladder hyperplasia	−	++	−
Adrenal cortical atrophy (*zona glomerulosa*)	−	++	−
Hemorrhage			
Intestinal	+	+	−
Adrenal	−	++	−
Ascites	++	−	+
Cutaneous lesions	−	−	+++

[a] Data from Moore (20).

Other Effects. In one or more species of laboratory animals, bone marrow hypoplasia, testicular degeneration, renal pelvis and urinary bladder hyperplasia, and hemorrhage in the intestines and adrenals have been observed.

Enzyme Induction. 2,3,7,8-Tetra-CDD and other halogenated dibenzo-p-dioxins and dibenzofurans stimulate a number of enzyme activities, most notably in the liver (1). 2,3,7,8-Tetra-CDD is a potent inducer of hepatic and renal microsomal drug metabolizing enzymes (57-69). Intoxication with 2,3,7,8-tetra-CDD results in a marked increase in the cellular smooth endoplasmic reticulum content of hepatic and renal cells (60,69). 2,3,7,8-Tetra-CDD can simultaneously activate and suppress certain microsome-associated foreign-compound and steroid-hormone-metabolizing enzyme systems (63) as well as increase the activity of both renal and hepatic glutathione-S transferase (70).

2,3,7,8-Tetra-CDD is the most active of the PCDDs in inducing hepatic δ-aminolevulinic acid (ALA) synthetase and aryl hydrocarbon hydroxylase (AHH) in chick embryo liver preparations (71, 72).

The PCDDs that induce ALA synthetase in chick embryo have two common properties: (1) halogen atoms occupy at least three of the four ring positions (2,3,7,8), and (2) at least one free, nonhalogenated carbon atom is unoccupied (71). The available toxicological data (35) indicate that those PCDDs that are lethal at low doses, teratogenic, or produce acne also induce ALA synthe-

Table 4. Evaluation of reported embryotoxic and teratogenic effects induced by 2,3,7,8-tetrachlorodibenzo-p-dioxins in rats and mice[a]

Species	Strain	Embryotoxic/ teratogenic effect	Dose, μg/kg Lowest Tested[b]	Dose, μg/kg ED_{50}[c]	Period of dosing, days	Route	Reference
Rat		Intestinal hemorrhage	0.125	0.57		Oral	*(50)*
	CD	Kidney abnormality	0.5	>1	6–15	S.C.	*(45)*
Mouse	CD-1	Cleft palate	1?				
			3	>3	6–15	S.C.	*(45)*
		Kidney abnormality	1	1–3	6–15	S.C.	*(45)*
	DBA/2J	Cleft palate	3	>3	6–15	S.C.	*(45)*
		Kidney abnormality	3	>3	6–15	S.C.	*(45)*
	C57BL/6J	Cleft palate	3	>3	6–15	S.C.	*(45)*
		Kidney abnormality	3	<3	6–15	S.C.	*(45)*
	NMRI	Cleft palate	3	6.5	6–15	Oral	*(46)*
			9	<9	9–13	Oral	*(46)*
			15	40	13	Oral	*(47)*
			5	15	11	Oral	*(47)*

[a] Data from Neubert et al. *(47)*.

[b] The lowest dose with which an embryotoxic or teratogenic effect detectable at birth has been produced is indicated. Since sometimes only one dose level was tested, this does not necessarily represent the lowest dose from which an effect could result.

[c] ED_{50}-dose required to produce an embryotoxic effect in 50% of animals.

tase; those PCDDs that are not toxic generally do not induce ALA synthetase. The structure-activity relation of PCDDs to induce AHH in chick embryos was identical to that in inducing ALA synthetase *(71)*.

Mixed-function oxidase enzyme systems of mouse strains "non-responsive" to other aromatic hydrocarbons were induced by single doses of 2,3,7,8-tetra-CDD, as evidenced by increases in hepatic monooxygenase activities and in concentrations of cytochrome P-448 *(73-76)*. Genetic resistance to induction of AHH by 3-methylcholanthrene in DBA/2J mice was overcome by treatment with 2,3,7,8-tetra-CDD. This result conflicts with the hypothesis that induction of AHH activity is a consequence of the formation of cytochrome P-448 *(77)*. A component that has a high binding affinity for 2,3,7,8-tetra-CDD was found in mouse liver cytosol *(78)*.

2,3,7,8-Tetra-CDD induces AHH even in 'poorly responsive' strains of mice *(79)*, not only in liver but also in lung, kidney, and colon. The DBA/2N strain, which responds only weakly to the sarcomatogenic action of 3-methylcholanthrene, becomes highly susceptible after treatment with 2,3,7,8-tetra-CDD *(74, 80)*.

2,3,7,8-Tetra-CDD is approximately 30,000 times more potent than 3-methylcholanthrene in inducing AHH activity in rat liver *(81)*.

McConnell et al. *(18)* reported that the comparative toxicity of 13 PCDDs in mice and guinea-pigs (see Table 2) supports the idea that the relative potency (or rank order) of a congener to produce one toxic response is a good indicator of its relative potency (or rank order) to produce other toxic manifestations.

Hepatic Cytosol Binding Protein. A macromolecular binding species has been characterized in the hepatic cytosol fraction of mouse and rat liver which has the *in vitro* binding properties predicted for the receptor for the induction of AHH activity based on the *in vivo* biology *(78)*: namely, (1) ^{3}H-2,3,7,8-tetra-CDD binds to this cytosol protein reversibly with a high affinity (K_d = 0.27 n*M*) comparable to the ED_{50} for hepatic AHH induction (ED_{50} in mice = 1 nmole/kg); (2) the binding affinity of halogenated dibenzo-*p*-dioxins and dibenzofurans for this protein *in vitro* corresponds to their potency to induce hepatic AHH activity in the chicken embryo; and (3) other compounds, such as the polycyclic aromatic hydrocarbons, which induce AHH activity and cytochrome P_1-450 also compete for this cytosolic binding protein, but compounds which induce other types of microsomal monooxygenase activities (e.g., phenobarbital) and steroids fail to bind. Thus, this cytosolic binding protein may be the receptor for the induction of AHH activity.

Structure-Activity Relations. The pathologic effects produced by the toxic PCDD and PCDF isomers are similar to those of 2,3,7,8-tetra-CDD for a given species, differing only in the intensity of the toxic effect produced by a given isomer. The toxic PCDDs have chlorine atoms in at least three of the four lateral ring positions (2,3,7, and 8) with at least one unsubstituted ring position (the octa-CDD is comparatively inactive). To the extent that the toxicity has been determined, a similar structure-toxicity relation has been observed for the PCDFs.

The structure-activity relation established for PCDDs and PCDFs for the induction of hepatic aryl hydrocarbon hydroxylase (AHH) activity and for binding to the hepatic cytosol binding species has been extended to other classes of chlorinated aromatic compounds. 3,4,3′4′-Tetrachloroazoxybenzene (TCAOB) and 3,4,3′,4′-tetrachloroazobenzene (TCAB) are potent acnegens formed as trace contaminants in the synthesis of 3,4-dichloroaniline or herbicides based on this compound (*82*). At high doses in animals, TCAB is reported to produce thymic involution and liver damage similar to 2,3,7,8-tetra-CDD (*83*). Both TCAOB and TCAB are potent inducers of hepatic AHH activity and bind to the hepatic cytosol binding protein with a high affinity. Congeners such as 3,5,3′5′-tetrachloroazoxybenzene and 3,5,3′,5′-tetrachloroazobenzene fail to induce AHH activity, fail to bind to the hepatic cytosol species, and fail to produce chloracne.

Of 16 halogenated biphenyl compounds tested, only 3,4,3′4′-tetrachloro-, 3,4,5,3′4′5′-hexachloro- and 3,4,5,3′4′5′-hexabromobiphenyls induced hepatic AHH activity and bound to the hepatic cytosol binding species (*84*). The 3,4,3′4′-tetrachlorobiphenyl has been reported to produce chloracne. McKinney et al. (*56*) found that of five hexachlorobiphenyls tested in chickens, 3,4,5,3′4′5′-hexachlorobiphenyl was by far the most toxic, and the only one that induced significant chick edema and involution of the thymus.

Pharmacokinetics. In the rat, following acute or chronic administration, 2,3,7,8-tetra-CDD is accumulated primarily in the liver and to a lesser extent in the fat, and is largely eliminated unmetabolized in the feces with a whole body half-life of about 3 weeks. Some pharmacokinetic experiments suggest the formation of a polar metabolite appearing in the urine, but direct attempts to demonstrate metabolism with hepatic microsomes *in vitro* have been negative (*1*).

Mutagenicity. Only four dioxin isomers have been evaluated for mutagenicity: the 2,7-di-, 2,3,7,8-tetra, and octa-CDDs as well as the unsubstituted dibenzo-*p*-dioxin (*85*).

2,3,7,8-Tetra-CDD increased the reversion frequency to streptomycin independence in *Escherichia coli* Sd-4. In *Salmonella typhimurium*, frameshift mutations in strain TA1532, but not base substitutions in strain TA1530, were induced by toxic concentrations of 2,3,7,8-tetra-CDD (*86*). In plate assays, the response was positive with *S. typhimurium* TA1532, doubtful with TA1531 and TA1534, and negative with G46 and TA1530 (*87*). McCann (*88*) tested 2,3,7,8-tetra-CDD in *S. typhimurium*, both with and without metabolic activation, using a spot-test and the standard plate test with strains TA1532, TA1535, TA1537, and TA1538; all these tests were negative.

Octa-CDD was nonmutagenic in *S. typhimurium* strains G46, TA1530, and TA1531, and doubtful results were obtained with strains TA1532 and TA1534 (*87*). Metabolic activation systems were not included in any of these microbiological assays.

Inhibition of mitosis and chromosomal abnormalities (dicentric bridges and chromatin fusion with formation of multinuclei or a single large nucleus) were observed in endosperm cells of the African blood lily (*Haemanthus Katherinae* Baker) treated with 2,3,7,8-tetra-CDD in the presence or absence of 2,4,5-T (*89*).

No chromosomal aberrations were observed in bone marrow cells of male rats treated with 2,7-di-CDD, 2,3,7,8-tetra-CDD, or dibenzo-*p*-dioxin by oral intubation, with 2,3,7,8-tetra-CDD by intraperitoneal injection or orally (*90*). However, when Osborne Mendel rats of both sexes were treated twice weekly for 13 weeks with 2,3,7,8-tetra-CDD, a significant but weak increase in the number of chromosome aberrations in bone marrow cells was reported (*91*).

2,3,7,8-Tetra-CDD did not induce dominant lethal mutations in Wistar rats after oral administration to males for 7 days (*51*).

Carcinogenicity. Two reports indicate that chronic administration of low levels of 2,3,7,8-tetra-CDD to rats is associated with an increased incidence of neoplasia (*1, 92, 93*).

Groups of 10 male Sprague-Dawley rats were fed a diet containing 2,3,7,8-tetra-CDD for 78 weeks in the following amounts (figures in parentheses are approximate weekly doses): 0, 1 ppt (0.0003 μg/kg body weight) 5 ppt (0.001 μg/kg), 50 ppt (0.01 μg/kg), 500 ppt (0.1 μg/kg), 1 ppb (0.4 μg/kg), 5 ppb (2.0 μg/kg), 50 ppb (24 μg/kg), 500 ppb (240 μg/kg), and 1000 ppb (500 μg/kg). The three highest dose levels (50, 500, and 1000 ppb) were toxic and killed all animals by the fourth week. Of the six remaining test groups, the overall incidence of neoplasms was 23/60 (38%); none occurred in the 1 ppt group. In the 5 ppt group, 5/10 animals had 6 neoplasms [ear-duct carcinoma, lymphocytic leukemia, adenocarcinoma, malignant histocytoma (with metastases), angiosarcoma, Leydig-cell adenoma]; the following groups also showed neoplasms: 50 ppt, three observed in 3/10; 500 ppt, four 4/10; 1 ppb, five observed in 4/10; 5 ppb, ten observed in 7/10. Neoplasms were not observed in the controls (*92*).

Groups of 100 Sprague-Dawley rats (50 males and 50 females) received for two years diets containing 0, 22, 210, and 22,000 ppt, equivalent to 0.0, 0.001, 0.01, and 0.1 μg 2,3,7,8-tetra-CDD/kg/day. Continuous ingestion of 0.001 μg/kg/day did not cause any chemically related changes in tumor incidence or toxicity; feeding with 0.01 μg/kg/day induced an increased incidence ($p < 0.05$) of hepatocellular hyperplastic nodules (female: 18/50 versus 8/86 controls), of focal alveolar hyperplasia in the lungs, and of urinary excretion of porphyrins (female). Dietary intake of 0.1 μg/kg/day caused an increased incidence ($p < 0.05$) of hepatocellular carcinomas (female: 11/49 versus 1/86) and squamous-cell carcinomas of the lung (female: 7/49 versus 0/86), of the hard palate/nasal turbinates (male: 4/50 versus 0/85; female: 4/49 versus 0/86), and of the tongue (male: 3/50 versus 0/85). Further increased were adenoma of the adrenal cortex (male) and hepatocellular hyperplastic nodules (female). At this dose, certain age-related lesions were reduced (males: acinar adenoma of the pancreas; females: granulosal cell neoplasm of the ovary, benign and malignant tumors of the mammary gland, pituitary adenoma, and benign tumors of the uterus). Also, chronic administration of 2,3,7,8-tetra-CDD caused multiple toxicologic effects, including increased mortality, decreased body weight gain, slight depression of certain hematologic parameters, increased urinary excretion of porphyrins and δ-aminolevulinic acid, increased serum levels of alkaline phosphatase, glutamyl transferase and serum glutamic pyruvic transaminase, and morphologic changes primarily of the hepatic, lymphoid, respiratory, and vascular tissues of the body (*93*).

These two reports show that chronic administration of 2,3,7,8-tetra CDD causes an increased incidence of neoplasms, but not whether 2,3,7,8-tetra-CDD acts as an initiator or promoter. This consideration is particularly important because unequivocal evidence is lacking that 2,3,7,8-tetra-CDD is a mutagen or is metabolized, and no evidence is available that 2,3,7,8-tetra-CDD and/or metabolite(s) bind covalently to macromolecules.

As summarized in Table 5, at least 24 long-term carcinogenicity studies on mice and rats are in progress (*94*).

Humans

Toxic Effects in Humans. Toxicity due to 2,3,7,8-tetra-CDD has been reported after occupational exposure during the industrial synthesis of 2,4,5-trichlorophenol (TCP) and 2,4,5-T, after exposure in factories and in the surrounding environment due to accidents occurring during the synthesis of TCP, and after exposure to herbicides and other materials containing 2,3,7,8-tetra-CDD. Exposed subjects have been found to develop a wide variety of lesions and symptoms (Table 6). For instance, a typical exposure victim experiences a number and a variety of clinical signs and symptoms: early exposure symptoms may include a burning sensation of the eyes, nose, and throat followed by headache, dizziness, nausea, and vomiting. Some days later, severe itching, redness, swelling of the face, more marked over the eyelids, nose and lips, may develop. Within the initial weeks after exposure, inflamed nodules as well as pustules appear on the face, forearms, shoulders, neck, and trunk, leading then to comedones and cysts. After a month or two, acneform eruptions emerge and the skin becomes hyperpigmented. At about the same time, aching muscles, mainly in the thighs and chest area, become manifest and aggravated on exertion. Insomnia, extreme irritability, and loss of libido also occur during this stage.

Other than the consistently found clinical feature of acne, other findings in humans may include: neuromuscular symptoms (weakness and pain with nerve conduction abnormalities), porphyria cutanea tarda, hepatic dysfunctions, hyperlipidemia, cutaneous hyperpigmentation and hirsutism, chronic eye irritation, emotional disorders, and neuropsychiatric syndromes.

Chloracne, one of the most constant and prominent features of 2,3,7,8-tetra-CDD exposure, has been described as a refractory acne characterized by inclusion cysts, comedones and pustules, with eventual scarring of the skin, more frequently originating on the face and sometimes spreading to other parts of the body. Many patients also have blepharoconjunctivitis and irritation of other mucous membranes. Sometimes the chloracne is preceded by erythematous and edematous skin lesions. The latent period between exposure and the appearance of clear signs of chloracne ranges from a few weeks to several months (*106*).

An important and unique episode revolves around three scientists who were self-exposed to 2,3,7,8-tetra-CDD: one heated trichlorophenol in an alkaline solution, a second heated potassium trichlorophenate, and a third worked in the same laboratory as the second and used a diluted solution of the synthesized dioxin (*107*). The first two scientists developed chloracne eight weeks after exposure, whereas the third showed no evidence of the characteristic acneform lesions. Delayed symptoms, probably due to 2,3,7,8-tetra-CDD, developed approximately two years later, and the second two scientists showed personality changes

Table 5. Ongoing long-term carcinogenicity testing of chlorinated dibenzo-p-dioxins.[a,b]

Compound	Number of studies	Route	Species
Dibenzo-p-dioxin	4	Oral (diet)	Mouse, rat
		Skin	Mouse
			Mouse (with DMBA)[c]
2,7-Di-CDD	4	Oral (diet)	Mouse, rat
		Skin	Mouse
			Mouse (with DMBA)[c]
2,3,7-Tri-CDD	3	Oral (gavage)	Mouse, rat
		Skin	Mouse
2,3,7,8-Tetra-CDD[d]	5	Oral (diet)	Rat
		Oral (gavage)	Mouse
		Oral (gavage)	Mouse, rat
		Skin	Mouse
1,2,3,6,7,8-Hexa-CDD[d]	3	Oral (gavage)	Mouse, rat
		Skin	Mouse
1,2,3,7,8,9-Hexa-CDD[d]	2	Oral (gavage)	Mouse
		Skin	Mouse (with 1,2,3,6,7,8-hexa-CDD)
1,2,3,4,6,7,8,9-Octa-CDD	3	Oral (diet)	Mouse, rat
		Skin	Mouse

[a] Data taken from Information Bulletin on the Survey of Chemicals Being Tested for Carcinogenicity, No. 7 (96). Details of these studies as well as the authors/institutes are available in this source reference document.

[b] As of October 1979, carcinogenesis bioassay testing within the National Toxicology Program included unsubstituted dibenzo-p-dioxin (UDD; CAS 262-12-4; NCI Tech. Rept. No. 122), considered not carcinogenic to Osborne-Mendel rats and B6C3F1 mice when administered in feed at dose levels of 5 and 10 ppb, and 2,7-dichlorodibenzo-p-dioxin (DCDD; CAS 33857-26-0; NCI Tech. Rept. No. 123), considered not carcinogenic to Osborne-Mendel rats and female B6C3F1 mice but suggestive of a carcinogenic effect in male B6C3F1 male mice when fed concentrations of 5 and 10 ppb. Studies are in progress on 1,2,3,6,7,8-hexachlorodibenzo-p-dioxin (HCDD, CAS 57653-85-7) and 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD: CAS 1746-01-6) by gavage to Osborne-Mendel rats and B6C3F1 mice and by skin painting on Swiss mice. Testing on 2,3,7,8-tetrachlorodibenzofuran (TCDF; CAS 51207-31-9) is to begin in fiscal year 1980. For chemical disposition studies octachlorodibenzo-p-dioxin, 2,3,7,8-tetrachlorodibenzofuran, and the stereochemically related 2,4,3',4'-tetrachloroazobenzene are also proposed.

[c] DMBA = dimethylbenzanthracene.

[d] The National Toxicology Program has completed and reported the results for the long-term carcinogenesis bioassay studies on 2,3,7,8-tetrachlorodibenzo-p-dioxin and 1,2,3,6,7,8-/1,2,3,7,8,9-hexachlorodibenzo-p-dioxins, with the following results.

2,3,7,8-tetrachlorodibenzo-p-dioxin—gavage, carcinogenic for Osborne-Mendel rats (increased incidences of follicular-cell thyroid tumors in males and of liver tumors in females) and carcinogenic for B6C3F1 mice (liver tumors in both sexes and thyroid tumors in females); dermal, carcinogenic for female Swiss-Webster mice (fibrosarcoma in the integumentary system) and although not shown carcinogenic for male Swiss-Webster mice, an increase in the same tumor type was observed. Mixture of hexachlorodibenzo-p-dioxins—gavage, carcinogenic for female Osborne-Mendel rats (hepatocellular carcinomas or neoplastic nodules), carcinogenic for male and female B6C3F1 mice (hepatocellular carcinomas and adenomas), and not demonstrated as carcinogenic for male Osborne-Mendel rats; dermal—not considered carcinogenic for male and female Swiss-Webster mice.

(mainly loss of energy and drive); impairment of vision, taste, and muscular coordination; sleep disturbances; gastrointestinal symptoms; and hirsutism. The first of the three experienced none of these adverse effects. All three exhibited hypercholesterolemia (>300 mg/100 ml).

Human Exposure to PCDDs and PCDFs

Major sources of human exposure to PCDDs and PCDFs include: exposure in the workplace; exposure in factories and in the surrounding environment from industrial accidents; exposure to contaminated materials, wastes, or food in the general environment; and exposure in Vietnam and other intensive herbicide spraying operations. (Prior and subsequent to use as a defoliant, 2,4,5-T was used in weed-killing and forest-thinning operations in the United States of America and elsewhere).

Occupational exposure may occur in manufacturing plants producing chlorinated phenols (tri-, tetra-, and pentachlorophenols), or phenoxy acid herbicides (2,4-D, 2,4,5-T), or PCBs; in factories utilizing these chemicals for the production of other substances (hexachlorophene from 2,4,5-trichlorophenol); in factories manufacturing or repairing transformers and capacitors or having heat exchange or heat hydraulic systems containing PCBs; and in the use processes of these chemicals under various occupational conditions such as spraying of herbicides, using chlorinated phenols for a variety of applications (especially wood preservative), sawing, or otherwise processing treated wood, and using hexachlorophene in sanitary occupations.

Table 6. Toxic effects of 2,3,7,8-tetrachlorodibenzo-p-dioxins in humans.

Effects	References
Dermatological	
Chloracne	(25, 28, 96–108)
Porphyria cutanea tarda	(27, 104, 105, 109)
Hyperpigmentation and hirsutism	(27, 28, 107)
Internal	
Liver damage[a]	(27, 96, 98, 101, 102, 104–106, 110)
Elevated serum hepatic enzyme levels	(27, 28, 96, 104–106, 110)
Disorders of fat metabolism	(28, 104, 107)
Disorders of carbohydrate metabolism	(28, 101, 102, 104, 106)
Cardiovascular disorders	(101, 102, 104, 105)
Urinary tract disorders	(97, 101, 102)
Respiratory disorders	(95, 101, 102)
Pancreatic disorders	(101, 102)
Neurological	
Polyneuropathies (peripheral neuritis)	(101, 102, 104, 106)
Lower extremity weakness	(28, 95, 99, 101, 102, 104, 105, 106)
Sensory impairments (sight, hearing, smell, taste)	(28, 101, 102, 107, 110)
Psychiatric	
Neurasthenic or depressive syndromes	(28, 95, 99, 101, 102, 104, 105, 107)

[a] Mild fibrosis, fatty changes, hemofuscin deposition and parenchymal-cell degeneration were observed in a few cases.

The burning of materials impregnated with commercial 2,3,4,6-tetrachlorophenates yielded 150-1000 μg of mixed PCDDs/g chlorophenate. Although only found as a minor constituent, 2,3,7,8-tetra-CDD has been quantified at levels exceeding 10 μg/g chlorophenate (*111*).

Pyrolysis of a technical grade PCB mixture yielded many PCDF isomers; the total yield could be as high as 3–25%. One of the main constituents is 2,3,7,8-tetra-CDF, the most toxic PCDF-isomer. Consequently, uncontrolled burning of PCBs can be an important environmental source of the hazardous PCDFs, and operations such as welding or soldering electrical equipment containing PCBs, or using casting waxes in foundries, may possibly entail a significant exposure (*112*). A PCB used in a heat exchange system for two years contained approximately 1.25 ppm of 2,3,7,8-tetra-CDF and a total of 15 ppm of PCDFs (*113*).

Apart from accidents such as the one which occurred in Seveso in 1976, general environmental exposure may originate from herbicide spraying and waste disposal.

An outbreak of PCDDs poisoning in humans, horses, and other animals occurred in Missouri in 1971 (*97, 114*) following the spraying of contaminated oil for dust control in horse arenas.

Another possible source of exposure to PCDDs and PCDFs pollution are waste oils, and possibly other waste, when burned both in industrial and municipal incinerators. Under simulated environmental conditions, the combustion of a standard 2,4,5-T formulation led to formation of small amounts of PCDDs and PCDFs (*115*). Buser and Bosshardt (*11*) quantified the total amount of PCDDs and PCDFs in fly ash from an industrial incinerator heating facility as 0.2 and 0.1 ppm, and in the fly ash from an industrial heating facility in Switzerland as 0.6 and 0.3 ppm. More than 30 individual PCDDs can be identified in the fly ash, but the known highly toxic PCDD isomers are only minor constituents (*12*). The number of PCDF isomers was larger; but, in this case, the known highly toxic isomers are major constituents (*13*).

An additional potential source of human exposure has been revealed: beef fat taken from cattle grazed on 2,4,5-T-treated rangeland contained 2,3,7,8-tetra-CDD; of the 11/14 positive samples, the four with the highest levels had 12, 20, 24, and 70 ppt (*10*). In another study, 3 of 24 samples of beef fat contained 3–4 ppt 2,3,7,8-tetra-CDD (*116*). Moreover, in a preliminary report of an ongoing enlarged study of women living in areas where 2,4,5-T is used on rangeland, 4/18 breast milk samples each contained approximately 1 ppt (*10*).

Workers in wood processing industries are exposed to wood dust containing preservatives as well as accompanying impurities and degradation products. Wood dust from a saw-mill in which a 2,3,4,6-tetrachlorophenol formulation was used as a fungicide was found to contain 1-10 ppm PCDFs and <0.5 ppm PCDDs (*15*).

In 1968, more than 1200 persons in South-west Japan were intoxicated by consuming a commercial rice oil contaminated with 1000 ppm PCBs. Nagayama et al. (*117*) analyzed the rice oil (Yusho oil) and found 5 ppm PCDFs, the major constituents of which were tetra- and penta-CDFs. Buser et al. (*113*) recently showed that 2,3,7,8-tetra-CDF was the main PCDF in the Yusho oil (0.45 ppm). The high level of PCDFs was caused by leakage from heat exchangers containing PCBs contaminated with PCDFs.

Workers manufacturing 2,4,5-trichlorophenol (TCP) or 2,4,5-T during normal production operations, and/or following explosions taking place in these plants, may have been exposed to a variety of polychlorinated chemicals whose type and quantity depends on the particular chemical processes in use and on the phase of the reaction in which the accident took place. Apparently, for instance, PCDFs are produced in the earlier stages when mainly tetrachlorobenzene is present and PCDDs are produced nearer the end of the reaction when primarily trichlorophenol is extant. The concentration of chlorophenols and chlorobenzenes, for example, was probably higher in the 1963 episode in The Netherlands, where the accident took place at the beginning of the reaction, then in the 1968 episode in the United Kingdom, or the 1976 accident in Italy, where the explosion took place at the end.

A thorough description of the reported industrial accidents and other cases of intoxications observed in exposed workers is given in the IARC Monograph (*1*). In this present report, only those episodes specifically discussed at length by the NIEHS/IARC *ad hoc* Working Group will be considered. (A sequential perspective of known accidents is given in Table 7).

In 1949, the first reported cases of industrial poisoning due to the formation of 2,3,7,8-tetra-CDD in uncontrolled exothermic reactions occurred during the manufacture of 2,4,5-trichlorophenol at a 2,4,5-T-producing factory in Nitro, West Virginia; 228 persons were affected (*99, 118*). In November 1953, an accident occurred in Ludwigshafen, Federal Republic of Germany, during the manufacture of TCP (*101,102,119,120*); 53 workers were affected by chloracne.

Five cases of chloracne were reported following an industrial accident in an Italian TCP-producing factory (*121*). In 1963, an accident occurred at the 2,4,5-T-producing factory in The Netherlands; approximately 50 persons were affected by chloracne (*122, 123*). In 1966, Dugois et al. (*98*) observed 21 cases of chloracne after an accident in a French factory producing TCP in the Grenoble region. In 1968, an accident occurred at the TCP-producing factory at Bolsover, Derbyshire, United Kingdom (*103, 106*). Within the next 7 months, 79 workers developed chloracne. In 1971, 2,3,7,8-tetra-CDD contaminated waste oil caused an outbreak of poisoning in humans, horses, and other animals (*97, 124*). In July 1976, an accident at the TCP-producing factory in Meda, Italy (*96*) resulted in the contamination of a large, densely populated area, including the towns of Seveso, Meda, Cesano Maderno, and Desio.

Key information concerning the effects of human exposure to herbicides in Vietnam, especially to the so-called "Agent Orange" (a 50:50 mixture of the *n*-butyl esters of 2,4-D and 2,4,5-T, containing up to 30 mg/kg or more 2,3,7,8-tetra-CDD), may be found in the literature (*1, 110, 125–127*).*

Exposure Episodes Considered in Detail by the NIEHS/IARC *ad hoc* Working Group

The text below is a condensed version of the discussions which took place during the two-day NIEHS/IARC *ad hoc* Working Group Meeting.

Phenoxy Acids Exposure

Cohort studies on herbicide sprayers have been conducted or are being planned in Scandinavian countries. The more advanced of these concerns Swedish railroad workers with exposure to a variety of herbicides. These people exhibited a significantly increased tumor incidence (apparently dose-dependent) and tumor mortality (*129*). The excess of tumors was found particularly among workers with exposure to amitrole (aminotriazole), whereas those exposed to phenoxy acids (2,4-D and 2,4,5-T) showed only a slightly increased excess of cancers. The study was small-sized, comprising 2978 person-years at observation in the total cohort and with 18 deaths *versus* 20.54 expected. The original conclusion from this study was that amitrole exposure may have caused an excess of tumors, whereas there was probably no pertinent increase in tumor incidence associated with exposure to phenoxy acids. The study has been recently reanalysed using a case-control approach, and through stratification on amitrole when considering the effect from phenoxy acids, and *vice versa*. The results show a possible and previously masked tumor-inducing effect also from phenoxy acids.

Another retrospective cohort mortality study, conducted in Finland on workers of five companies involved in spraying 2,4-D and 2,4,5-T on brushwood, did not show any increase in mortality. During 1955–1971, in the younger group of workers (under 45 years of age), however, four cancer deaths were observed versus less than two expected (no statistically significant difference). A prospective follow-up study for the period 1972-1976 revealed fewer cancer-related deaths than expected in all age groups. Clinical and anamnestic investigations were also performed showing a picture of acute complaints during and following the spraying operations: headache, transient dizziness, fatigue, abdominal complaints, skin and mucous irritations, and a few cases of persistent papulae.

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* More than 2,000,000 gallons of Agent Orange remaining from military defoliant operations were destroyed by incineration on board ship in the Pacific Ocean, 120 miles from Johnston Island. Temperatures not lower than 1250°C were used. The steel containers were melted (*128*).

Interestingly, some samples of 2,4,5-T used in Finland for spraying operations contained from 0.04 to 0.07 ppm 2,3,7,8-tetra-CDD. This may imply that the 2,4,5-T produced before 1965 contained lower levels of 2,3,7,8-tetra-CDD impurities than has been observed subsequently from 2,4,5-T used elsewhere. However, the analytical methods used in the determination of 2,3,7,8-tetra-CDD in the Finnish samples were antiquated in view of the rapid advancements made in analytical methodology and thus a confirmatory analysis of the samples using modern techniques was made by Rappe et al. (*130*). Five samples of 2,4,5-T ester dating from 1962 to 1967 were analysed for PCDDs and PCDFs; levels of 0.1-0.95 ppm 2,3,7,8-tetra-CDD and 0.1-0.15 ppm tetra-CDF were found.

A second feasibility study was designed and conducted in Finland to determine whether one could obtain anamnestic, clinical, hematological, and immunological information on Finnish railway and forestry workers who had been exposed for several years to herbicides containing 2,3,7,8-tetra-CDD. The exposed group consisted of 30 men who were control-matched to persons of the same age coming from the same district with similar job backgrounds and living conditions. Of the tests made, including liver and immunofunction studies, no differences were observed between the exposed and control groups. Although the population study is too small to permit any general conclusions as to the potential adverse health effects from long-term exposure to phenoxy acids, the investigation shows that follow-up is possible on the health status of persons exposed for several years to 2,3,7,8-tetra-CDD-containing phenoxy acids, and then to compare the exposed group results to carefully matched controls. The study is in progress.

Hexachlorophene Exposure

An excess of malformations, some severe, has been reported among children whose mothers were employed as nurses in a hospital. The mothers were exposed to hexachlorophene soap during early pregnancy, and the hypothesis of a causal relation between such an exposure and the occurrence of the malformations has been advanced (*131*); five severe and six slight malformations were observed in 65 children in the exposed group, whereas only one slight malformation was observed in the 68 children of the unexposed group. This report has been followed by another study (to be published) of a similar group of children of exposed mothers in comparison to children of unexposed mothers. Again a high frequency of malformations among the offspring of exposed mothers was reported (*132*). From these studies, however, it is not clear if exposure to other hazardous chemicals could be excluded. A retrospective-prospective study is being initiated among long-term workers of an United States' factory which used Seveso-produced 2,4,5-trichlorophenol in the manufacture of hexachlorophene. However, in the case of hexachlorophene, polychlorinated xanthenes have been also identified as contaminants at a higher level than 2,3,7,8-tetra-CDD (*133*).

Phenoxyacids and Chlorophenols Exposure in Forestry and in Wood Industry Workers

At the Regional Hospital in Umea (Northern Sweden), Hardell (*134*) observed that several patients suffering from mesenchymal tumors reported occupational or other exposures to phenoxyacids. More specifically, 87 mesenchymal tumors were diagnosed during the years 1970 through 1976. Of these cases, 55 were men (more than expected) and 43 of these 55 men were known by profession: 19 were either forestry workers, farmers and forestry workers, or workers in sawmills and papermills where exposure to chlorophenols is common. Based on the official statistics of Sweden, one can calculate approximatively the expected fraction of tumors within these trades, resulting in an expectancy of approximately 11 cases versus the 19 observed.

The Mount Sinai School of Medicine in New York is currently planning a field survey on long-term health effects on wood-preservative workers in Arkansas and Oklahoma in the United States of America.

Exposure to 2,3,7,8-Tetra-CDD during Production of 2,4,5-T or Polychlorinated Phenols and Following Industrial Accidents

The following cases, as well as others not considered at the meeting, have been described in IARC Monographs Volume 15 (*1*), and only some of the previously available information will be given here. The ongoing epidemiological studies on these cohorts are summarized in Table 7.

As each individual cohort has a relatively small number of person-years, a study has been proposed in which all the cohorts would be pooled and the mortality compared to that expected from the national statistics.

The first reported cases of industrial poisoning due to the formation of 2,3,7,8-tetra-CDD in uncontrolled exothermic reactions occurring during the manufacture of TCP were seen in 1949 at a 2,4,5-T-producing factory in Nitro, West Virginia, USA; 228 persons were affected. These individuals were studied by Suskind and Ashe (*135*) and followed up for a period of four years. Symptoms included chloracne, nausea, vomiting, headaches, severe muscular aches and pain, fatigue, emotional instability, and intolerance to cold. Laboratory findings showed raised total lipids and raised prothrombin time. Among those affected were not only workmen, but also laboratory personnel, medical personnel, and even the Safety Director who visited the areas of exposure. Several wives who had never visited the plant also developed acne, usually at the same time as their employee husbands.

It is important to note that information on the toxicity as well as on the stability (long persistence and slow degradability) of 2,3,7,8-tetra-CDD was not available at the time the first reports of acute toxicity were observed, and no measures were taken to decontaminate the factories and control the residue levels of 2,3,7,8-tetra-CDD. In fact, the presence of 2,3,7,8-tetra-CDD or other PCDDs and PCDFs was not even suspected. Workers, therefore, were probably exposed for a considerable time to 2,3,7,8-tetra-CDD following the first observations of acute toxic effects.

In November 1953, an accident occurred at a TCP factory in Ludwigshafen, Federal Republic of Germany; 75 workers were exposed to the reaction products during the accident and the subsequent cleaning work; most were affected by chloracne, 42 severely: 21 of the 42 suffered consequent damage to internal organs or disturbances of the nervous system. The most relevant features were polyneuritis, sensorial impairments, and liver damage. The son of one of the workers developed chloracne following contact with his father's work clothes. An additional case of poisoning occurred 5 years later in a worker who was involved in repair work (welding one of the auto-claves) at the contaminated site; subsequently this worker died with necrotic pancreatitis.

All the 75 workers could be traced in a cohort study 25 years later; mortality was compared both with the regional and national mortality and with a control group of workers from the same factory. In the exposed group, 17 deaths were observed (11 to 25 expected depending on the control population); six from cancer (four or less expected), five from cardiovascular diseases (as expected), two from suicides (0.2-0.6 expected), one from liver cirrhosis, one from a urogenital tract disease, and two from traffic accidents.

Of the six cancer deaths, three were from stomach cancer and occurred in the age group of 60-69, which is significantly more than expected. This effect was more pronounced when a minimum observation period of 10 years was considered, and more so for stomach cancer after a 20-year observation period. (Use of a long observation period permits a better estimation of the relation between exposure and disease when long "latency" periods are involved, as for cancers).

A similar accident occurred at the 2,4,5-T-producing factory in The Netherlands in 1963; 106 men are likely to have been exposed to 2,3,7,8-tetra-CDD (and possibly PCDFs) as they were in the building where the accident occurred during the subsequent period, March-July 1963. These workers may be divided into three groups: (A) factory employees (exposed during all phases of the cleaning and reconstruction activities), 44 men; (B) clean-up crew (nonfactory personnel, exposed during the months May-July), 18 men; and (C) plumbing, painting, and insulating personnel (nonfactory workers, exposed during the months May-July), 44 men.

During the explosion in Amsterdam, two operators were present in the building. With the exception of these men, who were probably exposed primarily by the inhalation route, all other workers used safety masks and were probably exposed by dermal contact. Chloracne was the most common and prominent lesion observed following 2,3,7,8-tetra-CDD exposure (26/ examined in group A, 10/16 in group B, and 8/16 in the group C). Liver function tests (thymol turbidity and serum glutamic pyruvic transaminase and serum glutamic oxaloacetic transaminase) did not indicate liver damage. A few men complained of fatigue. The latent period between exposure and the appearance of chloracne, characterized by comedones, pustules, and cysts on the face and sometimes on other parts of the body, was approximately 4-6 weeks. Sometimes, erythematous and edematous skin lesions, possibly due to phenolic compounds, were noted one day after exposure. No skin lesions (chloracne) were reported in family members of the employees. Of group A, 3/44 workers died, one of pancreas carcinoma in 1964, one of myocardial infarction at the age of 69, and one of a traffic accident. Of the 17/18 traced individuals in the B group, four have died (three from sudden death, probably of myocardial infarction, at ages 41, 53, and 55, and one of ill-defined pulmonary or cardiac cause at age 44). Only 32/44 of the C group were traced, and one of them died of sudden death, probably myocardial infarction, at age 50.

Jirásek et al. (*104, 105, 109*) studied 55 subjects from a cohort of 78 workers from a factory in Czechoslovakia producing 2,4,5-T and pentachlorophenol, who were affected by chloracne. The workers were probably exposed during the years 1965-1968 to unknown levels of 2,3,7,8-tetra-CDD. A significant symptom was the disturbance in porphyrins metabolism with signs of porphyria cutanea tarda. Many workers also suffered severe hepatic and neurological damage and had raised blood levels of cholesterol and total lipids. In the first years of follow-up, five deaths were observed, two from bronchogenic carcinoma at age 47 and 59 (only 0.12 lung cancer deaths were expected from national mortality statistics), one from atypical atherosclerosis at age 57, and one from the acute occupational intoxication. One further death, probably from liver cirrhosis, has recently been observed and 50 workers are still being followed. Many workers continue to show lipemia and hypercholesterolemia and have developed prediabetic changes and hypertension. The workers lost to follow-up are mostly foreigners who returned to their country of origin.

In July 1976, an accident in a TCP-producing factory in Meda, Italy resulted in the contamination of the towns of Seveso, Meda, Cesano Maderno, Desio, Nova Milanese, and possibly others of a large, densely populated area called the Brianza di Seveso with a total population of about 220,000 inhabitants. A retrospective health survey conducted on the workers of the ICMESA factory revealed that two workers among those directly involved in the production of 2,4,5-trichlorophenol suffered from skin lesions previous to July 1976. These facts may be indicative of a previous 2,3,7,8-tetra-CDD exposure.

A large and intensive follow-up program is in progress in the Seveso area; data were presented about the first dermatological, neurological, clinical, and laboratory findings, as well as about fetal damage. Dermatological examinations, including the screening of 32,000 children, resulted in the finding of hundreds of children with skin lesions, 135 of which were eventually identified as chloracne; 59 cases were from the more contaminated area (Zone A). However, precise description of diagnostic criteria and accurate anamnestic information, including, among others, data on places of residence, were not included. This information is needed before evaluating the meaning of the chloracne incidence data by territorial areas and efforts should be made obtain it. Chloracne cases were not systematically searched for in adults. Neurological examinations showed both signs of subclinical neurological damage and cases of clinically detectable polyneuropathy in adults (34/338 persons from zone A and 8/185 from the surrounding areas).

In about 30% of 1654 adults from both A zone and nearby zones, hepatomegaly was reported to be present on clinical investigation. No information, however, is given on the criteria by which the hepatomegaly was evaluated. The same percentage of abnormalities was observed in one or more liver tests (mainly glutamyl transferase and serum glutamic pyruvic transaminase and serum glutamic oxaloacetic transaminase). Extensive monitoring of various hematological parameters from 25,000 persons is now in progress and the data are expected to become available during 1978. Results of this investigation should allow a better understanding as to whether or not these alterations are caused by exposure to 2,3,7,8-tetra-CDD and PCDDs.

So far, immunological investigations, cytogenetic research, and embryomorphology analyses on cases of therapeutical abortions have not given abnormal results. However, the study of the frequency of congenital malformations and spontaneous abortions seems to be very difficult to accomplish. The importance of a systematic study on this subject has been stressed by the Working Group, because the questions on the teratogenicity of 2,3,7,8-tetra-CDD in humans cannot be solved by any other study.

A preliminary mortality study has been possible in 2 of the 11 towns of the Seveso area. The 1975-1977 mortality rates from liver cirrhosis and leukemia in these two limited zones of the Seveso area were compared to that of a nearby area (province of Varese). Within an overall mortality which did not appear different, an increase of deaths from liver cirrhosis and from leukemia was noted. The validity and significance of these observations should be carefully evaluated.

Recommendations

A chemical analytical program should be encouraged to identify and standardize analytical

Table 7. Epidemiological studies on 2,3,7,8-tetrachlorodibenzo-*p*-dioxin; human exposure episodes caused by accidental or occupational exposure occurring in factories producing 2,4,5-trichlorophenol and/or 2,4,5-trichlorophenoxyacetic acid.

Town and country	Year of exposure	Number of exposed persons	Clinical follow-up and cohort studies	Observations to date	Proposed actions	Comments and recommendations of the NIEHS/IARC Working Group
Accidental exposures						
Nitro, West Virginia, (U.S.A.)	1949	228	Only 36 individuals were followed, for a period of 4 years	No significant long-term observations are yet available (some followed-up individuals had symptoms of severe intercostal neuritis	Mortality cohort study being planned	Efforts should be made to trace the individuals who were exposed, possibly through the employment compensation files.
Ludwigshafen/Rhein, Federal Republic of Germany	1953	75	A mortality cohort study has conducted 24 yr after the accident; all exposed workers were traced for a total of 1525 person-years of observation	6 Cancer deaths were observed: 3 of stomach cancer in the age group 60-69 (significantly higher than expected), 2 of oat-cell carcinoma of the lung, and 1 of colonic adenocarcinoma	Follow-up to be continued	The results of the continuing follow-up study should periodically be made available.
Amsterdam, The Netherlands	1963	106	Preliminary observations on mortality are available; 63 exposed workers have been traced up to 1977	Of 8 deaths, 5 or 6 were from cardiovascular diseases, 5 probably from myocardial infarctions; the myocardial infarction death rate seems higher in the most heavily exposed workers affected by chloracne. One worker, who did not develop chloracne, died from pancreatic carcinoma 14 months after the accident; however, he complained of abdominal pain prior to the accident	Full report planned for 1978	Efforts should be made to trace all the workers who were exposed.
Bolsover, Derbyshire, United Kingdom	1968	90	Of the workers belonging to the original cohort, 50% are still employed and routinely undergo clinical and laboratory investigations	One worker is known to have died from coronary thrombosis	Epidemiological cohort study to be planned when the results of the present clinical follow-up investigation become available	Efforts should be made to trace all the workers who were exposed.

Meda, Brianza di Seveso, Italy	1976	?[a]	A clinical follow-up of the inhabitants from the more contaminated areas is being carried out. At the time of the accident, living in Zone A was a population of 730 people, with 200 of those being between 0-14 years of age. Of these 730 persons, 623 (125 between 0-14 years of age) were followed-up. Zone B contained a population of 4732 inhabitants with 1293 between the ages 0-14 years. An accurate count of those followed in Zone B is not available, but 943 youngsters between 0-14 years of age are included in the follow-up	Initial clinical observations showed a high incidence of 2,3,7,8-tetra-CDD-dependent skin lesions among children living in the more contaminated area. Also, a number of persons residing in the zone surrounding the more contaminated areas had skin lesions, but with poorly defined, clinical features; these lesions may be the result of 2,3,7,8-tetra-CDD exposure. Moreover, both clinical and laboratory findings suggest an increased incidence of hepatic sufference among adults living [illegible] the highly contaminated [illegible]. A preliminary mortal[illegible] study suggests that al[illegible] the overall rates [illegible] Seveso towns are not [illegible] from a nearby area, [illegible] ease of deaths from [illegible] cirrhosis and leukemia was noted	Among other ongoing investigations, a long-term morbidity study has been initiated	Possible teratogenic and other adverse reproductive and developmental effects from 2,3,7,8-tetra-CDD exposure should be investigated. A mortality register and population files, suitable for adequate descriptions of morbidity data, should be established. Further, the cancer registry that already covers a nearby province, should be extended to include the Seveso area.
Occupational exposure Czechoslovakia	1965-1969	80	A follow-up has been made regularly on 55 workers of the original cohort. The workers lost to follow-up are mainly foreigners who left the country	Five patients died during the first 5 year-follow-up period: 2 died from bronchogenic carcinoma and 1 from a rapidly developing atypical atherosclerosis. One further death, probably from liver cirrhosis, has recently occurred. Many of the workers are now suffering from hypertension and show signs of hyperlipidemia and hypercholesterolemia as well as prediabetic symptoms and signs	Follow-up to be continued. A 10-year report will be prepared during 1978	The results of the continuing follow-up study should periodically be made available.

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[a] No reliable information was available to the Working Group about the actual number of exposed persons; the entire area has a population of approximately 200,000 people.

methods used, to catalogue products contaminated with PCDDs and PCDFs, and to establish a register of known PCDD and PCDF standard samples.

The Working Group unanimously recommended that a system be developed for an international exchange of information and research coordination on the health effects of chlorinated dibenzo-*p*-dioxins/chlorinated dibenzofurans. Further, and in particular, the following three areas were indicated as deserving special attention:

1. Development of sensitive and reliable measurements of body burden; improved, more sensitive, and less expensive analytical technology should be generated. Standardized sampling (air, water, soil, tissues and body fluids, environmental), preparation, clean-up, and analysis should be promoted;

2. Development of common protocols for clinical examinations (including reproductive experience) and, in particular, design of a protocol for basic core information;

3. Development of an international registry of exposed persons to serve as a basis for long-term follow-up: this was considered especially important because the relatively small size of populations involved in individual exposure episodes are an obstacle to risk assessment and thus pooling of data is almost a necessity.

The Working Group recommended that IARC explore the technical and financial feasibility, possibly in cooperation with other national and/or international organizations, of setting-up such a permanent mechanism which could include as a minimum starting program: (a) a periodical, perhaps biennial, meeting to up-date the progress of ongoing studies, and to identify needed developments; (b) an exchange of relevant information accruing during the interval between meetings; and (c) a register of chloracne cases, containing simple, essential information in a standardized form. This PCDDs/PCDFs exposure-related sign may help to better define an exposed cohort population suitable for long-term follow-up.

This report represents the views and opinions of the U.S. NIEHS/IARC (National Institute of Environmental Health Sciences/International Agency for Research on Cancer *ad hoc* Working Group which met January 10-11, 1978 in Lyon France to review the history of human exposure to these chemicals, to collate current information, and to plan and forecast needed new directions. The meeting was funded jointly by NIEHS and IARC.

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Conference Call with Dow - Friday

Don Kagel - Dow   Dave Kee - EPA
(?) - Dow   Myself - "

Draft report given to Dow by Hernandez to comment upon

Comments by Dow
cities comparable ?
Hooker/Canadians relationship
Bay of Fundy
Horse Flesh (?)

- Believe Report Title should be changed - not all sources covered
- Alsea study -- critical - want criticisms of the study included (But some industrially backed)
-- Agent orange - want these out
- Don't want comment on reduced fertility / 2,4,5-T connection - or their study in report
- Want the six lines (page 12) indicating risk modified (Dow concluded that no risk existed - want us to include diff. position). Critical of EPAs conclusions ("Dow's discharge represents major, if not only source of TCDD ----")
Kee (- will think about it, not receptive)

Question - Why is dioxin greatest in Gull Eggs at Saginaw Bay? - response - coal fired power plant !!!

[illegible] ... report!)

[illegible]

Replacement Language (page 12)

Based upon these findings, EPA judged in (month), 1978 that environmental contamination of PCDDs existed. In EPA's view this constituted a substantial risk of injury to the environment as defined under section 8(e) of TSCA. [illegible] In contrast Dow had previously concluded their environmental data did not demonstrate a section 8(e) risk. In preliminary assessments conducted in (month) 1978 it was determined that the plant's discharge represented the major source if not the only source of TCDD contamination found in the Tittabawassee and Saginaw Rivers and Saginaw Bay in Michigan. In these preliminary assessments it was concluded that no other information other than purely circumstantial was submitted by Dow to support the premise that PCDDs and especially TCDDs are typical byproducts of combustion. The assessments emphasized that the most probable source of PCDDs in combustion processes, including incinerators, would be from the burning of materials containing polychlorinated phenols or related compounds. [illegible]

More recent studies indicate that Dow Chemical may not be the only contributor to TCDD contamination observed in the Saginaw River basin.

EPA's 1978 study on fish from the Saginaw River Basin determined the presence of 2,3,7,8-TCDD in fish samples collected above Dow's discharge. Dow also reported in 1979 that fish collected from the Flint, Cass, and Shiawassee Rivers were positive for TCDD and other PCDDs. Dow attributed these results to combustion sources present along the river and not from pesticide production.

Language out - all six lines on page 12 - no replacement language at all (Kee wanted them out, because said Adamkus wanted shorter, less controversial language - not my interpretation. All names removed from report - (too compromised, no content)

8/10/81 Dave explains to Kovalick that lines taken out because - would take too long to discuss, could not resolve language with Dow - report needed to get out

WASHINGTON, D.C. 20460

(18)

NOV 05 1979

OFFICE OF TOXIC SUBSTANCES

Larry D. Edmonds, M.S.P.H.
Birth Defects Branch
Bureau of Epidemiology
Building 1, Room 5115
Center for Disease Control
Atlanta, Georgia 30333

Dear Larry:

Enclosed you will find the second draft of the design for our planned birth defects study in Midland. Please note the following changes:

1. (p.6) The calculation of confidence intervals has been omitted. Miettinen's method is based on the chi-square statistic and therefore would never yield a result at variance with the significance level. More important, however, is the fact that confidence intervals are inappropriate when a one-tailed hypothesis is being tested.

2. (p.2) I agree there is no apparent reason to exclude members of plural births from the study group. This variable can be recorded and inspected during analysis. [illegible]

3. (p.2) I have retained the exclusion of low birthweight children from the control pool. The decision, it seems to me, should be whether or not to include them among the cases. What is your advice?

4. (p.2) I have removed sex of child as a matching factor. Although some types of birth defects occur more frequently in children of one sex than the other, there is no reason to expect an association between sex of child and parental exposure (residential or occupational). Sex of child should consequently not be a confounding factor. Again, if the chi-square shows a statistically significant sex difference between cases and controls, adjustment or stratification can be employed (see pp.6-7).

5. (p.2) The age, race and gravidity (or parity) of the mother are strongly associated with many types of birth defects and are also likely to be associated with parental exposure. Gravidity or parity should have an association with exposure that is separate from that of age because of the greater likelihood of a nulliparous woman to be employed (e.g., at Dow Chemical), regardless of her age.

6. (p.5) Although this study was prompted by information received in connection with proceedings relating to 2,4,5-T and TCDD, it would not be scientifically sound to restrict the hypothesis solely to those substances--given the large number of chemicals used and manufactured at Dow Chemical's Midland facility. I have therefore added paragraphs to that effect to both the study design and the discussion of hypothesis formation (p.6).

7. (p.7) I have also added paragraphs briefly describing the second stage of analysis (by type of birth defect, job site, chemical exposure, etc.) and further data collection to be considered if positive results ensue from this initial analysis (e.g., confirmation of parental residence at conception, etc.).

8. I have deleted references to the study by Poland *et al.* (1971), which I mistakenly took to be a study of Dow's Midland plant. It was actually a study of a Newark, New Jersey plant of the Diamond Alkali Company (Firestone D. 1978. The 2,3,7,8-tetrachlorodibenzo-*para*-dioxin problem: a review. In: Ramel C. ed. Chlorinated phenoxy acids and their dioxins. *Ecol Bull (Stockholm)* 27: 39-52).

I would appreciate your further comments and wish to thank you again for your continued assistance on this project.

I am sending a copy of this draft to Dr. Wilcox and Mr. Van Amberg in Michigan, together with a request for a meeting to discuss the study. I will advise you upon receiving their response.

In the meantime, if you have a blank copy of the birth certificate used in Michigan, please send it. It will be helpful in deciding what information will be available from this data source.

Sincerely,

Charles Poole

Charles Poole
Epidemiologist
Health Review Division (TS-792)

Enclosure

MEMORANDUM

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
CENTER FOR DISEASE CONTROL

TO The Record

DATE: December 13, 1979

ROM : Health Services Officer
Birth Defects Branch, BOE

UBJECT: Birth Defects in Midland, Michigan

On November 19, 1979, I attended a meeting in Ann Arbor, Michigan, to discuss a proposed study of birth defects in Midland, Michigan. Attending the meeting were Charles Poole of the Environmental Protection Agency who proposed the study, Kenneth Wilcox, M.D., State Epidemiologist, George Van Amburg, Director of Vital Records and myself.

The purpose of the meeting was to discuss the protocol for the study. After much discussion, a two-part study was agreed on. First, Michigan would evaluate residental exposure to the Dow plant in Midland, Michigan, both urban and rural exposure, during the period 1971-1974 for total birth defects. The second part would be an occupational study using cases and matched controls. A list of names will be given EPA of cases and controls to present to Dow to obtain employment history.

At this time, the study has no completion date but I assume that it will progress rapidly. If any positive results are obtained, there are plans for a more detailed case-control study with interviews of parents.

Larry Edmonds, M.S.P.H.
Larry Edmonds

OCT 04 1978

Case-control Study of Birth Defects in Midland County, Michigan

1. Hypotheses

The hypotheses to be explored by this study are that parental employment with the Dow Chemical Company, residence proximal to Dow's chemical production facility, or both, were associated with the bearing of malformed children in Midland County, Michigan, during the period 1971-1974. The primary basis for these hypotheses is the finding of an excess of birth defects in the county as a whole compared to the state of Michigan during this time period (see attached discussion).

The hypotheses will be tested by comparing all malformed infants born during 1971-1974 in Midland County with two comparison groups: a sample of infants born without deformities during the same period and, in a separate analysis, all malformed infants born in the county during the periods 1967-1970 and 1975-1978 combined. The first analysis will estimate the relative risk, during the period 1971-1974, of bearing a malformed infant between Midland County residents more and less likely to have been exposed to Dow's manufacturing processes. The second analysis will determine whether parents of malformed children born in Midland County during this period were more likely to have been exposed to Dow's manufacturing processes than during periods when the county's

OCT 04 1979

incidence of birth defects was not in excess (1967-1970 and 1975-1978).

2. Selection of Study and Comparison Groups

The study group (cases) will consist of all malformed children known to have been born during the period 1971-1974 to women residing in Midland County. The two comparison groups will also consist of children known to have been born to women residing in Midland County. The first (normal controls) will consist of a sample of children born during the study period (1971-1974) without deformities, four such children matched to each case on the basis of the age (14 or under, 15-19, 20-24, 25-29, 30-35 and over 35), race and gravidity of the mother. Children with birth weights less than 2,500 grams will be excluded from the normal control pool. The second comparison group (abnormal controls) will consist of all malformed children born to women residing in the county during the periods 1967-1970 and 1975-1978.

The Birth Defects Branch, Bureau of Epidemiology, Center for Disease Control, will assist in gaining access to birth certificates, hospital records, or both to provide the necessary data.

3. Data Collection

The following information will be needed for each case and control:

a. sex;

b. mother's race;

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c. number of mother's previous pregnancies;

d. mother's age;

e. father's age;

f. type(s) of birth defects;

g. birth weight;

h. mother's street address

If the source records do not contain the number of mother's previous pregnancies (gravidity), the number of previous children (parity) will be used. Any additional information of relevance available from the source records (e.g., birth certificates) will also be recorded.

If the source records use the International Classification of Diseases (ICD), the recorded congenital malformation codes will be used. If not, a trained nosologist will classify the malformations directly from the source records, using the most recent revision of the ICD.

Mother's street address will be used to determine proximity to the Dow facility. Dow and EPA Region V have performed monitoring studies of polychlorinated dibenzodioxins (PCDD) in and around the plant. If possible, the results will be used to construct zones of proximity, centered at the plant site. The Environmental Protection Agency Municipal Water Supply Inventory indicates that the only public water supply in Midland County is the Saginaw-Midland Water Authority, which draws its water from Saginaw Bay in Lake Huron. Dow monitoring has detected PCDD contamination in Saginaw Bay,

drawn in past?

OCT 0

possibly originating from the Midland facility. The inventory lists a 1970 total of 35,176 people served in Midland County by this water supply. The 1970 population of the city of Midland was 35,206, strongly suggesting that the public water service area is restricted to the city limits. This suggestion is further substantiated by the fact that, according to the County and City Data Book, there were 10,190 occupied housing units in the city of Midland; the inventory lists 10,765 public supply services (10,710 meters) in the county.

It is also apparent that the entire urban population of Midland County is restricted to the city of Midland. The County and City Data Book states that approximately 34,945 (54.8%) of the county's 63,769 people can be considered urban residents. This figure corresponds well with the 35,206 population of the city. Control for water supply can therefore be obtained as a consequence of controlling for urban residence (i.e., residence within the Midland city limits). This will be accomplished as much as possible in constructing the proximity zones and, to the extent necessary, by stratification or adjustment in the analysis.

Parental employment with Dow will be determined by forwarding to the company an alphabetical list of the names and addresses of the mothers and fathers of all cases and controls. Dow will be asked to identify those individuals on the list who have ever been employed at the Midland facility and, of these, the job titles, site locations within the plant, duration of employment at each job and site, and chemicals used or manufactured at those sites. Plant monitoring data and industrial hygiene information will also be obtained.

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It should be pointed out that, although this study was prompted by information received in connection with proceedings relating to 2,4,5-T and TCDD, it would not be scientifically sound to restrict the etiologic hypothesis solely to those substances--given the large number of chemicals used and manufactured at Dow Chemical's Midland facility. Comprehensive exposure-related information will consequently be sought for those cases and controls with a history of employment at the facility.

EPA's Office of General Counsel (James Nelson, Staff Attorney) will help ensure that all obligations under the Privacy Act for treating and handling the data in this study are fully met.

4. Analysis

The sample size for this study is necessarily limited by the four-year period (1971-1974) when Midland County's total birth defect ratio per 1,000 live births appeared to be in excess. Michigan Department of Public Health (MDPH) figures, based on birth certificates, indicate that 111 malformed children were born to mothers residing in the county during this period (see attached discussion). This number would probably be greater if hospital records were available to identify cases. Since the ratio of total birth defects to live births was elevated two to three times during this period, the abnormal controls (drawn from a time period twice as long) should number between 74 and 111. The normal control group will have four times as many members as the case group, approximately 444 births.

Samples of this size will make it difficult to perform separate analyses for specific types of birth defects. For instance, the MDPH data indicate that 15 cases of cleft lip and palate occurred during the period 1971-1974. Because this figure was three times higher than the number expected on the basis of state-wide experience, it is anticipated that only about 10 cases will be included among the abnormal controls. Data on specific types of malformations will be inspected, however, for striking trends and statistical tests appropriate for small sample sizes will be applied. No separation of defects into "major" and "minor" categories will be made. For the normal controls, analysis will begin with matched-pair odds ratios and will proceed to analysis of unmatched material if necessary. The role of chance will be assessed by significance levels based on the one-tailed, continuity-corrected chi-square statistic.

OCT 04 1973

In the analysis of the normal controls, three possible confounding factors will be controlled by matching: mother's age, race and gravidity. The distribution of such factors as father's age and sex of child will be compared between cases and normal controls by the two-tailed, continuity-corrected chi-square statistic and, if significantly different at $\alpha = .05$, will be controlled by stratification or adjustment. The same procedure will be followed for all five of these potential confounding factors in the analysis of abnormal controls.

[illegible] confounding possible. Sig- [illegible] difficult [illegible] analy- [illegible]

The basic analysis for comparison of cases with each group of controls will consist of five four-fold tables, considering all malformations without regard for specific type. Exposure measures in these tables will be: 1) mother employed by Dow; 2) father employed by Dow; 3) either parent employed by Dow; 4) mother's residence "close" to Dow's plant; 5) either parent employed by Dow and/or mother's residence "close" to Dow's plant.

how

Initial analysis will consequently use employment at or residence near the Dow Chemical facility *per se* as the exposure indicator. After this analysis, regardless of the results, specific job sites or chemical exposures will be examined in the same manner as specific birth defect types.

If positive results are obtained from this study, strong consideration will be given to further investigation. For instance, if parental residence shows an association,

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ascertainment of residence at conception (rather than at birth) might be necessary. Similarly, an association with employment (especially if refined to specific job locations or chemical exposures) might lead to a decision to obtain more specific and detailed plant monitoring or industrial hygiene data.

OCT 04 1975

Discussion of Hypothesis Formation

[illegible]

More than sufficient data exist in the experimental and epidemiologic literature to support the generation of the hypothesis that human exposure to TCDD increases the risk of bearing malformed offspring. The more specific hypothesis that exposures within or near Dow's Midland facility between 1970 and 1973 increased this risk emerges from the following information.

In a critique of an EPA study of spontaneous abortions in Oregon associated with the spraying of 2,4,5-T (1), Dow scientists employed data from a hospital in Midland, Michigan as a control for the Oregon study area. In the course of EPA's inquiry into the Midland area's suitability as a control area, data and information arose on birth defects in Midland County. These data warrant further exploration.

During the period 1965-1970, the ratio of total congenital malformations to live births in Midland County was comparable to that for the whole State of Michigan (2). Beginning in 1971, however, the ratio rose precipitously to a peak more than three times higher than the state figure (see Figure 1). The ratio remained elevated until 1975, when it declined a level again comparable to the statewide total. In 1972 and 1973, Midland County's rate was the highest in the state (3).

Dr. R. Gerald Rice, Chief of the Michigan Bureau of Personal Health Services, in a letter to Mr. Todd Mason of the Midland Daily News, stated his opinion that the increase in the overall rate was due to increased reporting of "minor deformities" (4). No criteria for distinguishing "minor" birth defects from "major" ones were stated in the Michigan Department of Public Health (MDPH) materials received by EPA thus far, but a newspaper article by Mr. Mason supplied by Dow (5) cites water-filled scrota, undescended testes, slight heart murmurs, webbed or deformed toes, and certain skin or muscle defects as falling into the "minor" category.

The MDPH also supplied figures for expected cases based on state rates for three specific types of birth defects: cleft lip and palate, urogenital defects, and heart anomalies (6). The Table lists the results, which show all three types to be in significant excess during the 1970-1974 period. It is important to note that malformations falling into each of these three categories, especially cleft lip and palate, have also been observed in the animal experiments testing the teratogenicity of TCDD (7).

It is possible that some of the "minor" defects listed in Mr. Mason's article contributed to the excesses seen in the table for urogenital and heart defects. No information has been made available, however, which would distinguish between increased reporting of these "minor" defects and their increased occurrence. The article, written in 1976, reported that, although local hospital staff regarded reporting as "more thorough than in the past," they could remember "no formal change in reporting policy or practice" (5). Cases of cleft lip and palate, the most commonly observed malformation in the animal studies of TCDD, are never classified as "minor" anomalies. An important point is that increased reporting of birth defects in Midland beginning in 1971 would not explain the subsequent decline seen in Figure 1 to a level which by 1975 was again comparable to that of the state in general.

The possibility exists that some environmental factor in the Midland County area was responsible for the observed peak in birth defects in that area. The consistency of the specific types of anomalies in excess with those seen in animal studies helps to raise TCDD as a candidate.

A second newspaper article by Mr. Mason outlined Dow's 1976 plans to study this increase (8). Dr. H. C. Scharnweber, Dow's medical director, stated that the company would send registered nurses to interview the wives of workers engaged in the manufacture of 2,4,5-T and pentachlorophenol. The interviews were to focus on spontaneous abortions and congenital malformations. On May 23, 1979, a Dow spokesperson described this study as "still in progress" (9).

Dow's unpublished report, "The Trace Chemistries of Fire - A Source of and Routes for the Entry of Chlorinated Dioxins into the Environment," (10) was submitted to the EPA under the requirements of Section 8(e) of the Toxic Substances Control Act, "Notice to the Administrator of Substantial Risk." One of Dow's conclusions, based upon their sampling and analysis, was that "Michigan Division pesticide production facilities are not measurable sources of the trace levels of chlorinated dioxins found in fish taken from the Tittabawassee River" (10). EPA's status report on the submission, however, disagreed with this conclusion (11). Pointing out that TCDD was found in fish downstream, but not upstream, of Dow's Midland plant, the status report concluded that "the available information...continues to suggest that Dow Chemical Company's Midland, Michigan plant represents the major, if not the only, source of TCDD contamination found in the Tittabawassee and Saginaw Rivers and Saginaw Bay in Michigan" (11). Noting also that "the levels of polychlorinated dibenzodioxins found in Midland are 2-4 orders of magnitude greater than those reported at other locations," the EPA evaluation characterized the Midland area as "a definite TCDD 'hot spot'"(11).

No data or information on production volume, manufacturing processes, or possible environmental release of TCDD during the late 1960's and early 1970's were included in Dow's report. EPA information specialists have been asked to request such materials from Dow. It is known that Dow was a major supplier of TCDD-contaminated herbicides, primarily

OCT 04 1979

mixtures containing 2,4,5-T, used in massive quantities during the war in Vietnam (see Figure 2).

It was shortly after the announcement in April, 1970, of the suspension of certain 2,4,5-T uses by the Secretaries of Agriculture, Interior, and Health, Education and Welfare that the Department of Defense decided to abandon the use of 2,4,5-T as a defoliant in Vietnam (12). These decisions were in response to recently reported animal studies of the teratogenicity of TCDD.

It is also known that during the week preceding June 26, 1970, Dow export shipments from Bay City set a new record of six million pounds in five ships bound for "Europe, Latin America and the Far East" (13). Dow also announced at that time that shipments were 35% ahead of the previous year (13).

It was not until September of 1970 that Dow announced final completion of an $800,000 diversion system to keep spills of organic chemicals out of the Tittabawassee River and to "contain any spills within the Midland facility" (14).

The possibly accelerated production and/or shipment activity in the spring and early summer of 1970 at Dow's Midland plant, coupled with the installation of spill-containment capabilities in the fall of that year, suggest that a significant release of TCDD into the Midland County or Dow Chemical plant site environment during 1970 might have been possible. This possibility needs to be more fully explored.

It should be pointed out that, although the hypothesis relating excessive 1971-1974 birth defects in Midland County to the Dow Chemical facility was prompted by information received in connection with proceedings relating to 2,4,5-T and TCDD, it would not be scientifically sound to restrict attention solely to those substances--given the large number of chemicals used and manufactured at Dow Chemical's Midland facility. Comprehensive exposure-related information should consequently be sought for those cases and controls with a history of employment at the facility.

1. Blau G. E., Cook R. R., Gehring P. J., et al. Critique of "Report of assessment of a field investigation of six-year spontaneous abortion rates in three Oregon areas in relation to forest 2,4,5-T spray practices" by the Epidemiological Studies Program, Human Health Effects Monitoring Branch, Benefits and Field Studies Division, OPP, OTS, EPA. Paper submitted to the Environmental Protection Agency, March 5, 1979.

2. Michigan Department of Public Health. Data supplied to Dow Chemical Company, 1976.

3. Michigan Department of Public Health. Data supplied to the National Institute of Occupational Safety and Health, 1976.

4. Rice R. G. Letter to T. Mason supplied to the Environmental Protection Agency by the Dow Chemical Company, March 1979.

5. Mason T. Birth defect rate appears higher here. Midland Daily News, May 27, 1976.

6. Infante P. Proceedings: Conference on Women and the Workplace. Society for Occupational and Environmental Health, Washington, D. C., June 17-19, 1976, p. 139.

7. Van Ormer D. Personal communication. May 15, 1979.

8. Mason T. Dow to study miscarriage, birth-defects. Midland Daily News, May 28, 1976.

9. Leng M. L. Personal Communication, May 23, 1979.

10. The Chlorinated Dioxin Task Force, The Michigan Division, Dow Chemical U.S.A. Discoveries and conclusions excerpted from the report: "The trace chemistries of fire - a source of and routes for the entry of chlorinated dioxins into the environment." Paper submitted to the Environmental Protection Agency, 1979.

11. Kover F. Status Report 8EHQ-1178-0209 (supplement). Memorandum to Joseph J. Merenda, Director, Assessment Division, Office of Testing and Evaluation, Office of Toxic Substances, Environmental Protection Agency, February 8, 1979.

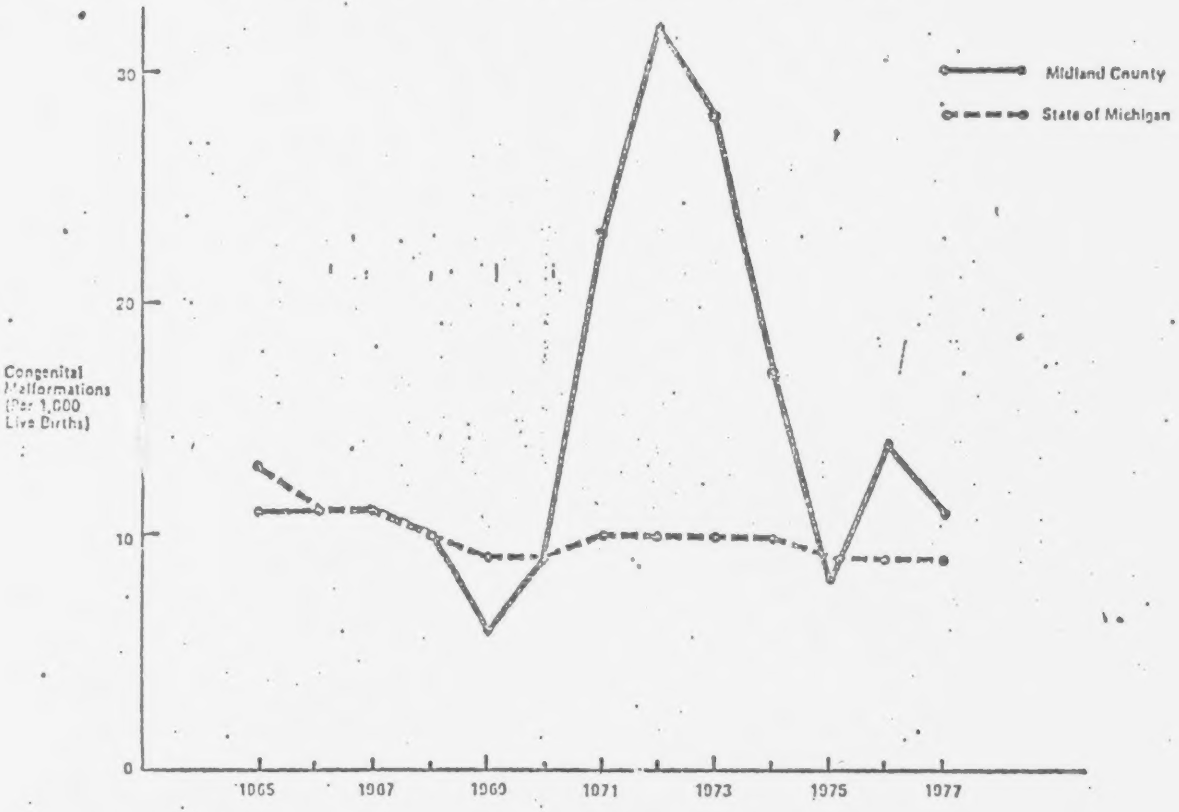
12. Young A. L. Calcagni J. A., Thalken C. E. and Tremblay J. W. The Toxicology, Environmental Fate and Human Risk of Herbicide Orange and Its Associated Dioxin. U.S. Air Force Technical Report OEHL TR-78-92, October 1978.

13. The Flint Journal, Flint Michigan, June 26, 1970.

14. The Flint Journal, Flint Michigan, September 5, 1970.

Figure I

TOTAL CONGENITAL MALFORMATION RATIOS IN STATE OF MICHIGAN AND MIDLAND COUNTY, 1965 — 1977



Source: Data supplied by Michigan Department of Public Health to Dow Chemical Company, 1978.

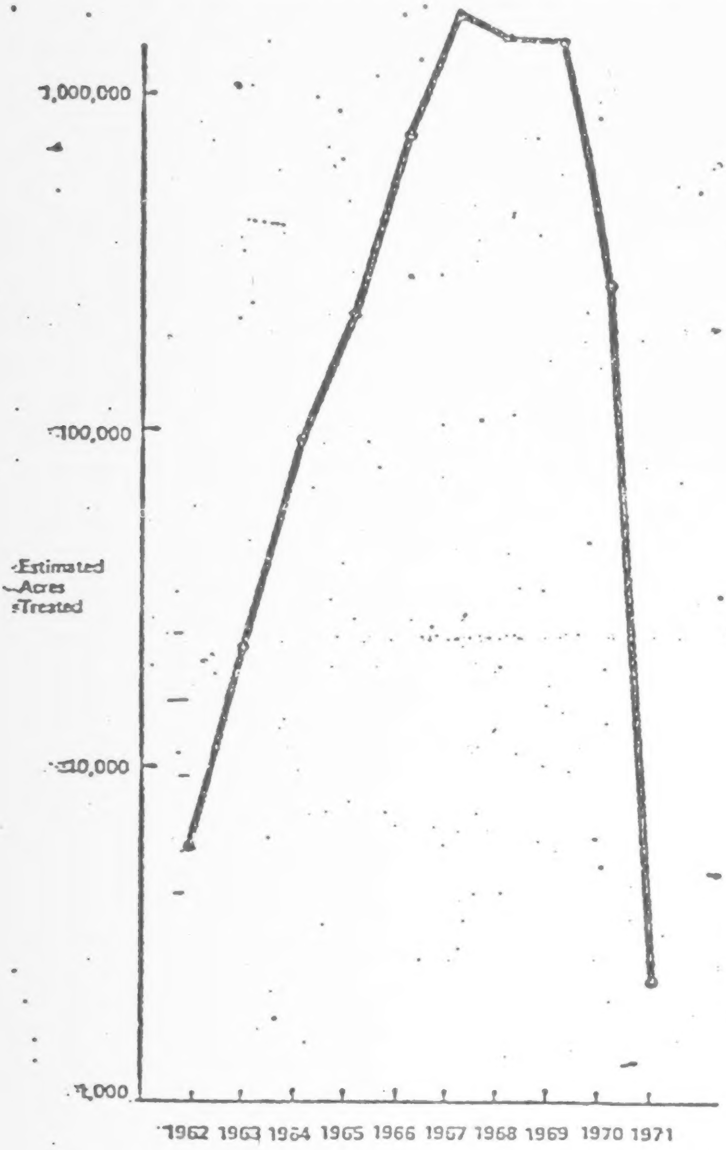
BIRTH DEFECTS IN MIDLAND COUNTY, MICHIGAN OBSERVED AND EXPECTED* CASES BY TYPE OF DEFECT 1970—1974

TYPE OF DEFECT	OBSERVED CASES	EXPECTED CASES	RATIO
Urogenital	34	7	4.9
Heart	12	4	3.0
Cleft lip and palate	15	5	3.0

*Expected cases derived from Michigan state rates.

Source: Data supplied by the Michigan Department of Public Health to the National Institute of Occupational Safety and Health, 1976.

USE OF HERBICIDES IN SOUTH VIETNAM 1962–1971



Source: Young AL, Calcagni JA, Thalken CE and Tremblay JW. The Toxicology, Environmental Fate, and Human Risk of Herbicide Orange and Its Associated Dioxin. U.S. Air Force Technical Report OEHL TR-78-92, October 1978.

EXHIBIT A

DOW CHEMICAL U.S.A.

June 8, 1983

MICHIGAN DIVISION
MIDLAND, MICHIGAN 48640

Gary E. Guenther, P.E.
Deputy Director
Department of Natural Resources
Stevens T. Mason Building
Box 30028
Lansing, MI 48909

Mr. Guenther:

Pursuant to your April 29, 1983, request for additional information regarding 2,3,7,8-TCDD levels in soil data submitted to you on April 23, 1983, the enclosed documents are being submitted. I am sure that you appreciate the sensitive nature of the location of the samples taken outside the Dow Plant. Please make every effort to keep this information confidential. We have no reason to believe that the levels of dioxin found at these locations will be different than what would be found at any other location in the city.

Response to the specific requests for information are:

1. The specific locations of the soil samples are shown on the attached maps (Attachment I and II).

2. The sampling protocol is as follows:

   Regarding ground soils: They were collected at the surface from open, undisturbed areas, 10 cm x 10 cm square and 1 cm deep on a sunny day (when possible), attempting to exclude grass and other debris. Each soil sample was placed in a clear-glass, 4-ounce, wide-mouth bottle (previously cleaned with RBS-35 in water and rinsed consecutively with water, methanol, acetone, and methylene chloride, the threads were then wrapped with teflon tape, and the bottle was equipped with a Poly-Seal cap) using a thoroughly cleaned stainless steel spatula.

   Regarding gutter soils: They were collected from the surface of concrete gutters where soil accumulation was maximum for the area. Approximately 100 cc of soil, excluding rocks and debris, were transferred to a sample bottle (same as above) using a thoroughly cleaned stainless steel spatula.

   The sealed soil samples were transported to the Analytical Laboratories where they were stored at ambient temperature, protected from light, until they were analyzed.

3. Both of the Midland soil samples were curbside dust. All but one of the Michigan Division soil samples were soil samples. P2-83 was a curbside dust sample taken from the curb just outside the fence of the Dow Plant.

4. Analytical Methodology: Soil samples examined in 1983 for isomer-specific TCDDs content were processed in accordance with the basic procedures described in Analytical Chemistry, 1980, 52, pp. 2045-2054 (attached), which includes validation data for a fortified sandy loam soil. A variety of modifications have been made upon these basic procedures to improve cleanup efficiency and CDDs sensitivity; these modifications are described in Analytical Chemistry, 1982, 54, pp. 2292-2299 (attached). Validation work describing fortification and recovery of all 22 TCDD isomers at low ppt concentrations in combustion-related particulate matter is described in this paper to include application of HRGC-LRMS quantitation on a Kratos MS-80 at a mass resolution of ~1000.

   The analytical procedure employed for the determination of isomer-specific TCDDs in soil samples has six basic steps: (1) TCDD removal from the sample matrix via benzene Soxhlet extraction; (2) gross impurity removal from the extract by chemically modified adsorbent treatments [i.e. silica gel, 44% (w/w) concentrated H_2SO_4 on silica gel), and 33% (w/w) 1N aqueous NaOH on silica gel]; (3) specialized adsorbent treatment of the remaining extract to remove common chemical interferences [i.e. 10% (w/w) $AgNO_3$ on silica gel and activated basic alumina]; (4) RP·HPLC residue fractionation to remove residual chemically similar interferences and to permit collection of TCDDs in three separate fractions which contain certain specific isomers and are free of most higher chlorinated CDDs; (5) silica-HPLC refractionation of each RP·HPLC TCDD fraction to produce a second high-efficiency, chromatographic separation having different selectivity to further remove residual interferents and to permit TCDD isomer specificity; and (6) HRGC-LRMS determination of TCDD isomers.

   Analytical Criteria for TCDD Identification and Quantification: The criteria for TCDD identification are: (1) correct RP·HPLC retention window for specific TCDD isomers, (2) correct silica-HPLC retention window for specific TCDD isomers, (3) correct isomer-specific retention time under isothermal HRGC conditions [±4 seconds absolute for TCDD isomer retention times between ~9 to 16 min.], (4) correct parent ion chlorine isotope ratio for native TCDDs at M/Z 319.896 and M/Z 321.893 at an instrumental mass resolution of ~1000 [±10% relative], (5) a signal intensity for each monitored mass ≥2.5 x peak to valley noise in an adjacent region of the mass chromatogram, and (6) a ^{13}C·2378·TCDD internal standard recovery

≥50% for each sample. Native TCDDs are quantified via an external standard procedure using peak heights. A primary calibration standard of native 2378·TCDD is used for quantification of all TCDD isomers. TCDD isomer recoveries for each sample have been shown to be nominally equivalent to that obtained for ^{13}C·2378·TCDD added to each sample as an internal standard, the recovery of which is also determined via an external standard procedure using peak heights monitoring M/Z 335.930. It should be noted that TCDD isomer quantification using this procedure may suffer some degree of inaccuracy for certain isomers because of variations in MS sensitivity; however, primary standards of most TCDD isomers are not currently available.

HRGC-LRMS Parameters for TCDDs: TCDD isomer identification and quantification are accomplished by HRGC-LRMS on a Kratos MS-80 equipped with a DS-55 data system operating in the multiple peak monitoring (MPM) mode: column, 0.20 mm ID x ~35 M fused silica capillary coated with a 0.17 µm film of SE-54 silicone; injector, an all quartz fractional splitter operated at ~320°C; helium carrier gas, ~30 cm/s linear velocity; fused silica open split interface, operated at ~275°C; source, operated in the electron impact ionization mode at ~300°C and ~2×10^{-6} torr; mass resolution, ~1000. TCDD isomers are analyzed at an isothermal column temperature of ~245°C. Native TCDDs are monitored at M/Z 319.896 and 321.893, and ^{13}C·2378·TCDD internal standard at M/Z 335.930.

The HRGC-LRMS linear response range for 2378-TCDD is examined at least twice per year for the MS-80 which is primarily dedicated to dioxin analyses. The instrument routinely demonstrates a linear response for TCDDs beginning at the limit of detection and proceeding to the range of ~800 pg injected. All sample residues are quantified at dilutions appropriate to maintain injected levels of TCDD isomers substantially less than ~400 pg.

Specific TCDD isomer fortification and recovery data for native isomers were not generated during this portion of the study. Reagent Blanks are run routinely among samples as a quality assurance procedure.

Limit of Detection (LoD): The limit of detection (LoD) for TCDD isomers is defined as 2.5 x peak to valley noise in an adjacent region of the mass chromatogram for specified TCDD ions monitored. The LoD is reported following observed level in parentheses whenever the observed value is <10 x LoD (i.e. <25 x peak to valley noise). The LoD is not reported if observed value is ≥10 x LoD.

The concentrations reported for observed values and LoDs for all TCDD isomers are corrected for the recovery of ^{13}C·2378·TCDD, which is included in each sample at an approximate concentration of 5 ng.

5. The four sites within the Dow plant which were covered with new soil since the 1978 sampling are samples 1A, 1B, 2A, and 2B, as shown in the 1983 data.

6. The 1978 results for the five sites within the Dow plant are attached (Attachment III).

7. The two samples collected from each of the several cities are from two distinct locations within the city. The 1983 samples are duplicates as far as possible of the earlier samples.

As to your request for other dioxin data, I am sure you are aware of the request from the EPA which will result in our compiling all of the data that Dow has. As D. T. Buzzelli told Paul Zugger on the telephone, we are responding to this request.

If you have further questions regarding the information enclosed, please contact me.

Sincerely,

V. T. May

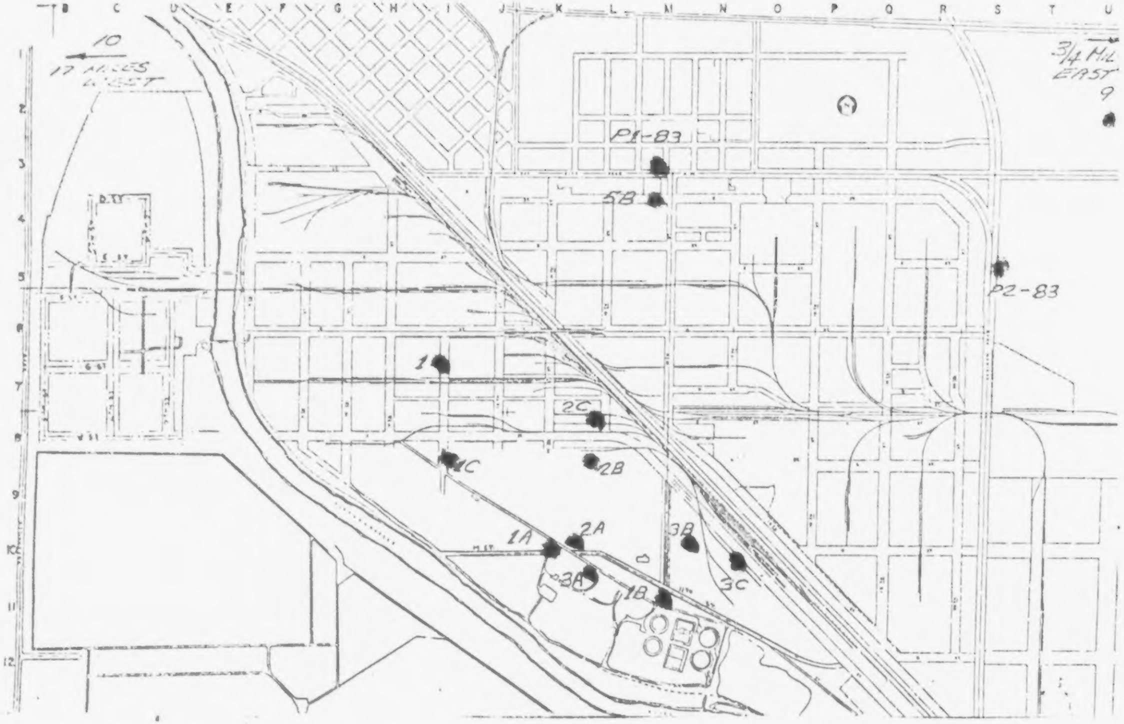
Vern T. May
Technical Director
1710 Building
(517) 636-3240

mh

Attachments

ATTACHMENT I

MICHIGAN DIVISION
SOIL SAMPLES


B C D E F G H I J K L M N O P Q R S T U
1 2 3 4 5 6 7 8 9 10 11 12
10
17 MILES WEST
3/4 MIL EAST
9
P1-83
5B
P2-83
1
2C
1C
2B
1A
2A
3B
3C
3A
1B

ATTACHMENT I

MICHIGAN DIVISION
SOIL SAMPLES
(1978)

CHLORINATED DIOXIN CONTENT OF SOIL SAMPLES

(Repeat from 1977 Soil Sample Locations)	Apparent Dioxin Concentration ng/g* (ppb)				
	TCDD				
Sample Number	Isomers	2,3,7,8-**	HCDD	H_7CDD	OCDD
1A	17	16	280	3200	20,500
1B	9	6	40	470	2,500
2A	18	100	120	650	6,300
2B	18	16	280	240	11,700
5B	0.8	0.3	7	70	490

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*ng/g means nanograms per gram.

**May contain as many as 11 isomers in addition to 2378.

ATTACHMENT I

MICHIGAN DIVISION
SOIL SAMPLES
(1977)

RESULTS	DIOXIN CONCENTRATION, ng/g (ppb)			
Sample #	Apparent TCDD*	Hexa*	Hepta	Octa
1A	1.5	6.2	12	140
2A	6	12	100	3100
3A	ND(1)	5	10	170
1B	2	5.5	33	450
2B	0.6	18	30	60
3B	ND(0.5)	ND(0.8)	4	11
1C	ND(0.4)	ND(2)	6.3	38
2C	ND(1.4)	ND(7)	1	10
3C	ND(0.1)	0.55	3.5	19
1	ND(1.2)	4	55	700
5B	ND(0.2)	1.1	11	100
9	ND(0.3)	0.36	18	160
10	ND(0.6)	ND(0.7)	2.8	38

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*May contain many isomers.

DIOXIN SOIL ANALYSIS
1983 ANALYSIS DATA

DOW PLANT

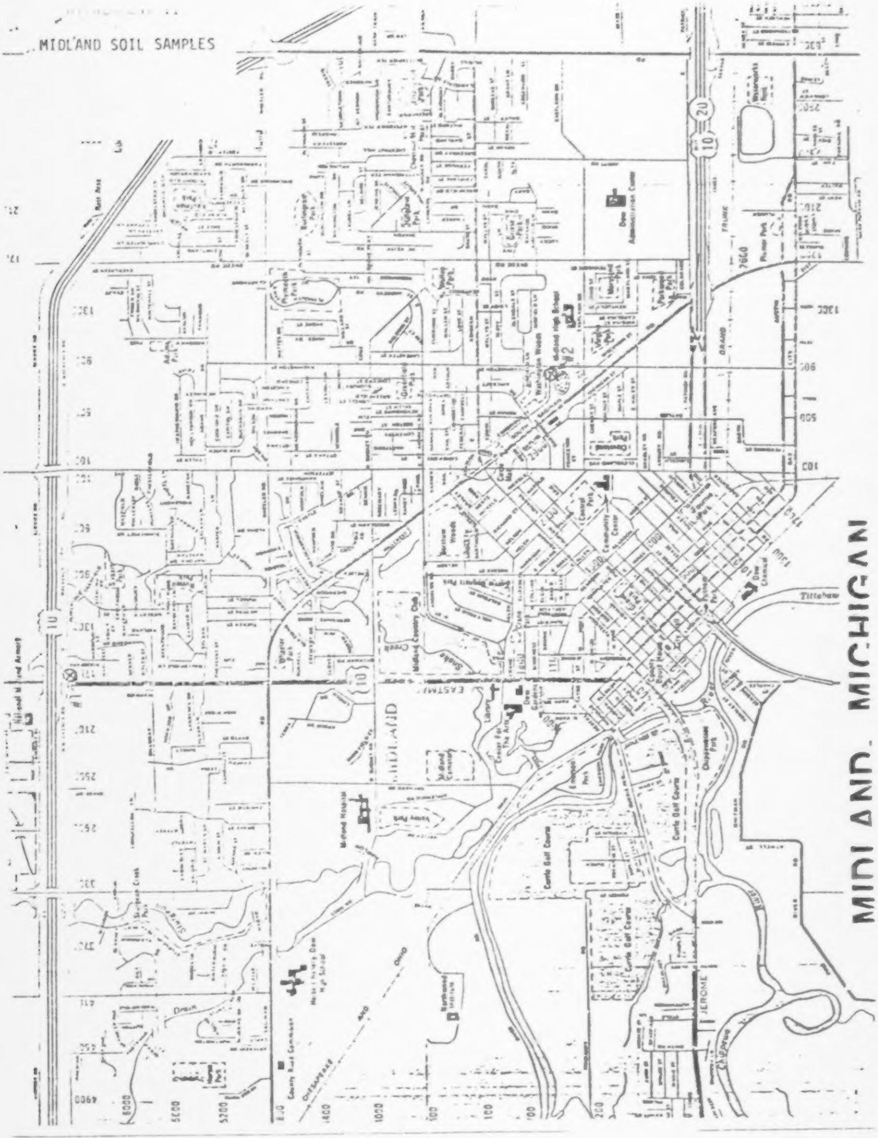
	Perimeter P1-83		Perimeter P2-83		1A		2A		1B		2B	
TCDD Isomer	PPB	(ng/g)	PPB	(ng/g)	PPB	(ng/g)	PPB	(ng/g)	PPB	(ng/g)	PPB	(ng/g)
1469-TCDD	0.0015	(0.0005)	0.0011	(0.0009)	0.0100	(0.0031)	0.0059	(0.0025)	nd	(0.0029)	nd	(0.0025
1269-TCDD	0.0016	(0.0005)	0.0030	(0.0009)	0.0213	(0.0031)	0.0132	(0.0025)	nd	(0.0029)	nd	(0.0025
1267-TCDD	0.0005	(0.0005)	0.0013	(0.0009)	0.0070	(0.0031)	0.0048	(0.0025)	nd	(0.0029)	nd	(0.0025
1289-TCDD	0.0008	(0.0005)	0.0027	(0.0009)	0.0134	(0.0031)	0.0095	(0.0025)	nd	(0.0029)	nd	(0.0025
1369-TCDD	0.0053		0.0085		0.0839		0.0271	(0.0050)	0.0033	(0.0029)	nd	(0.0017
1247+1248-TCDDs	0.0197		0.0416		0.288		0.172		0.0222	(0.0029)	0.0078	(0.0017
1278-TCDD	0.0059		0.0111		0.108		0.0498	(0.0050)	0.0086	(0.0024)	0.0029	(0.0017
1268-TCDD	0.0041		0.0118		0.0869		0.0420	(0.0050)	0.0055	(0.0029)	0.0024	(0.0017
1237+1238-TCDDs	0.0381		0.0555		0.964		0.284		0.0439		0.0186	
1279-TCDD	0.0093		0.0162		0.0832		0.0470	(0.0050)	0.0039	(0.0024)	0.0033	(0.0017
*1246-TCDD	0.0012	(0.0005)	0.0010	(0.0005)	0.0257		0.0095	(0.0039)	nd	(0.0029)	nd	(0.0021
1478-TCDD	0.0028	(0.0005)	0.0044	(0.0005)	0.0196	(0.0023)	0.0175	(0.0039)	nd	(0.0029)	nd	(0.0021
1236-TCDD	0.0027	(0.0005)	0.0039	(0.0005)	0.0433		0.0211	(0.0039)	0.0039	(0.0029)	nd	(0.0021
1239-TCDD	0.0008	(0.0005)	0.0023	(0.0005)	0.0227	(0.0023)	0.0075	(0.0039)	nd	(0.0029)	nd	(0.0021
*1249-TCDD	0.0019	(0.0007)	0.0030	(0.0006)	0.0323		0.0157	(0.0029)	0.0035	(0.0024)	nd	(0.0022
1368-TCDD	0.319		0.4800		3.700		2.130		0.682		0.0711	
1379-TCDD	0.0797		0.0729		1.040		0.248		0.155		0.0200	
1378-TCDD	0.0300	(0.0097)	0.0480		0.283	(0.030)	0.146		0.0182	(0.0031)	0.0075	(0.0015
1234-TCDD	nd	(0.0097)	0.0043	(0.0043)	0.033	(0.030)	nd	(0.014)	nd	(0.0031)	nd	(0.0015)
Total Other TCDD Isomers	0.5254		0.7734		6.8653		3.2506		0.9500		0.1336	
2378-TCDD	0.0810		0.0580		0.383		2.040		0.0184	(0.0027)	0.0219	
^{13}C·2378·TCDD Recovery:	74%		82%		70%		56%		51%		72%	

Explanatory Notes:

A. All TCDD isomers are determined by GC/MS using native 2378-TCDD as the primary reference standard.
B. All reported concentrations have been corrected for the observed ^{13}C·2378·TCDD internal standard recovery.
C. The limit of detection (values in parentheses) is defined as 2.5 x peak to valley noise in an adjacent portion of the mass chromatogram.
D. When observed signal is ≥25 x peak to valley noise, the limit of detection is not reported.
E. Samples 1A, 2A, 1B, and 2B were obtained from areas with new soil (since 1978) due to construction.

* Analytical methods don't allow for absolute confirmation that these two isomers are not reversed.

MIDLAND SOIL SAMPLES


MIDLAND, MICHIGAN
Dow Administration Center
Midland High School
Washington Woods
Community Center
Central Park
Dow Chemical
Tittabawassee
Midland Country Club
EASTMAN
MIDLAND
Midland Hospital
Dow Gardens
Center For The Arts
Emerson Park
Chippewassee Park
Currie Golf Course
Midland Airport
JEROME
Chippewa
Plymouth Park
Barstow Woods
Drain

ATTACHMENT II

MIDLAND
SOIL
SAMPLES
(1978)

CHLORINATED DIOXIN CONTENT OF DUST SAMPLES FROM MIDLAND, MICHIGAN

	Apparent Dioxin Concentration, ng/g (ppb)			
Sample Source	TCDD* Plus 11 Isomers	HCDD**	H_7CDD	OCDD
Midland, Sample 1	0.03(0.02)	0.2	2.3	19
Midland, Sample 2	0.04(0.02)	0.4	3.9	31

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[*] May contain 5 more isomers.

[**] May contain many isomers.

DIOXIN SOIL ANALYSIS
1983 ANALYSIS DATA

MIDLAND MICHIGAN

	#1		#2	
TCDD Isomer	PPB	(ng/g)	PPB	(ng/g)
1469-TCDD	nd	(0.0006)	nd	(0.0005)
1269-TCDD	nd	(0.0006)	nd	(0.0005)
1267-TCDD	nd	(0.0006)	nd	(0.0005)
1289-TCDD	0.0010	(0.0006)	nd	(0.0005)
1369-TCDD	0.0006	(0.0004)	0.0016	(0.0005)
1247+1248-TCDDs	0.0013	(0.0004)	0.0047	(0.0005)
1278-TCDD	0.0006	(0.0004)	0.0016	(0.0005)
1268-TCDD	0.0006	(0.0004)	0.0015	(0.0005)
1237+1238-TCDDs	0.0018	(0.0004)	0.0072	
1279-TCDD	0.0009	(0.0004)	0.0017	(0.0005)
*1246-TCDD	nd	(0.0007)	0.0005	(0.0005)
1478-TCDD	nd	(0.0007)	0.0007	(0.0005)
1236-TCDD	nd	(0.0007)	0.0005	(0.0005)
1239-TCDD	nd	(0.0007)	nd	(0.0005)
*1249-TCDD	nd	(0.0006)	nd	(0.0005)
1368-TCDD	0.0172		0.0365	
1379-TCDD	0.0033	(0.0009)	0.0127	(0.0014)
1378-TCDD	0.0018	(0.0009)	0.0054	(0.0014)
1234-TCDD	nd	(0.0009)	nd	(0.0014)
Total Other TCDD Isomers	0.0291		0.0746	
2378-TCDD	0.0016	(0.0006)	0.0072	
^{13}C•2378•TCDD Recovery:	67%		81%	

Explanatory Notes:

A. All TCDD isomers are determined by GC/MS using native 2378-TCDD as the primary reference standard.
B. All reported concentrations have been corrected for the observed ^{13}C•2378•TCDD internal standard recovery.
C. The limit of detection (values in parentheses) is defined as 2.5 x peak to valley noise in an adjacent portion of the mass chromatogram.
D. When observed signal is >25 x peak to valley noise, the limit of detection is not reported.

* Analytical methods don't allow for absolute confirmation that these two isomers are not reversed.

DIOXIN SOIL ANALYSIS
1983 ANALYSIS DATA

CHICAGO ILLINOIS

	#1		#2	
TCDD Isomer	PPB	(ng/g)	PPB	(ng/g)
1469-TCDD	nd	(0.0006)	0.0014	(0.0005)
1269-TCDD	nd	(0.0006)	0.0017	(0.0006)
1267-TCDD	nd	(0.0006)	0.0008	(0.0006)
1289-TCDD	nd	(0.0006)	0.0012	(0.0006)
1369-TCDD	nd	(0.0006)	0.0034	(0.0006)
1247+1248-TCDDs	0.0014	(0.0006)	0.0057	(0.0006)
1278-TCDD	nd	(0.0006)	0.0029	(0.0006)
1268-TCDD	0.0006	(0.0006)	0.0035	(0.0006)
1237+1238-TCDDs	0.0013	(0.0006)	0.0075	
1279-TCDD	nd	(0.0006)	0.0026	(0.0006)
*1246-TCDD	nd	(0.0006)	0.0010	(0.0006)
1478-TCDD	nd	(0.0006)	0.0013	(0.0006)
1236-TCDD	nd	(0.0006)	0.0012	(0.0006)
1239-TCDD	nd	(0.0006)	0.0008	(0.0006)
*1249-TCDD	nd	(0.0008)	0.0014	(0.0006)
1368-TCDD	0.0105		0.0884	
1379-TCDD	0.0052	(0.0006)	0.0181	
1378-TCDD	0.0017	(0.0006)	0.0094	(0.0016)
1234-TCDD	0.0006	(0.0006)	0.0030	(0.0016)
Total Other TCDD Isomers	0.0213		0.1553	
2378-TCDD	0.0010	(0.0007)	0.0042	
^{13}C·2378·TCDD Recovery:	63%		77%	

Explanatory Notes:

A. All TCDD isomers are determined by GC/MS using native 2378-TCDD as the primary reference standard.
B. All reported concentrations have been corrected for the observed ^{13}C·2378·TCDD internal standard recovery.
C. The limit of detection (values in parentheses) is defined as 2.5 x peak to valley noise in an adjacent portion of the mass chromatogram.
D. When observed signal is >25 x peak to valley noise, the limit of detection is not reported.

* Analytical methods don't allow for absolute confirmation that these two isomers are not reversed.

DIOXIN SOIL ANALYSIS
1983 ANALYSIS DATA

DETROIT MICHIGAN

	#1		#2	
TCDD Isomer	PPB	(ng/g)	PPB	(ng/g)
1469-TCDD	0.0005	(0.0005)	nd	(0.0007)
1269-TCDD	nd	(0.0006)	nd	(0.0007)
1267-TCDD	nd	(0.0005)	nd	(0.0007)
1289-TCDD	0.0008	(0.0005)	nd	(0.0007)
1369-TCDD	0.0023	(0.0005)	0.0026	(0.0004)
1247+1248-TCDDs	0.0029	(0.0005)	0.0055	
1278-TCDD	0.0018	(0.0005)	0.0030	(0.0004)
1268-TCDD	0.0016	(0.0005)	0.0038	(0.0004)
1237+1238-TCDDs	0.0055		0.0078	
1279-TCDD	0.0020	(0.0005)	0.0018	(0.0004)
*1246-TCDD	nd	(0.0006)	nd	(0.0007)
1478-TCDD	0.0006	(0.0006)	0.0007	(0.0007)
1236-TCDD	0.0008	(0.0006)	0.0008	(0.0008)
1239-TCDD	nd	(0.0006)	0.0008	(0.0008)
*1249-TCDD	nd	(0.0005)	0.0011	(0.0007)
1368-TCDD	0.0116		0.0485	
1379-TCDD	0.0065	(0.0010)	0.0229	
1378-TCDD	0.0061	(0.0010)	0.0089	
1234-TCDD	nd	(0.0010)	0.0011	(0.0008)
Total Other TCDD Isomers	0.0430		0.1093	
2378-TCDD	0.0036	(0.0007)	0.0021	(0.0004)
^{13}C·2378·TCDD Recovery:	80%		73%	

xplanatory Notes:

- All TCDD isomers are determined by GC/MS using native 2378-TCDD as the primary reference standard.
- All reported concentrations have been corrected for the observed ^{13}C·2378·TCDD internal standard recovery.
- The limit of detection (values in parentheses) is defined as 2.5 x peak to valley noise in an adjacent portion of the mass chromatogram.
- When observed signal is >25 x peak to valley noise, the limit of detection is not reported.

Analytical methods don't allow for absolute confirmation that these two isomers are not reversed.

ATTACHMENT III

SOIL SAMPLES OUTSIDE MIDLAND MICHIGAN

Sample Location	
Lansing #1	10x10x1 cm soil sample collected 18 MAR 83 from bare spot in Riverfront Park ~50 M east of Board of Water & Light Powerhouse
Lansing #2	Gutter soil collected 18 MAR 83 from concrete curb in southeast corner of Farmer's Market parking lot ~300 M east-northeast of Board of Water & Light Powerhouse
Chicago #1	Accumulated soil and dust from Cassen's Transport parking lot (concrete & asphalt) collected 19 MAR 83 from ~100 M northeast of Calumet Incinerator
Chicago #2	10x10x1 cm soil sample collected 19 MAR 83 from ~75 M northeast of Northwest Incinerator from bare spot in field ~40 ft. from railroad tracks
Detroit #1	10x10x1 cm soil sample collected 19 MAR 83 from Detroit River shoreline at foot of Southfield expressway between Jefferson Avenue and river
Detroit #2	10x10x1 cm soil sample collected 19 MAR 83 from ditch in Freedom Schoolyard carrying water away from Wayne County Incinerator ~100 M south of incinerator

DIOXIN SOIL ANALYSIS
1983 ANALYSIS DATA

LANSING MICHIGAN

	#1		#2	
TCDD Isomer	PPB	(ng/g)	PPB	(ng/g)
1469-TCDD	nd	(0.0007)	nd	(0.0007)
1269-TCDD	nd	(0.0007)	nd	(0.0007)
1267-TCDD	nd	(0.0007)	nd	(0.0007)
1289-TCDD	nd	(0.0007)	nd	(0.0007)
1369-TCDD	0.0005	(0.0004)	nd	(0.0008)
1247+1248-TCDDs	0.0021	(0.0004)	nd	(0.0008)
1278-TCDD	0.0007	(0.0004)	nd	(0.0008)
1268-TCDD	0.0004	(0.0004)	nd	(0.0008)
1237+1238-TCDDs	0.0012	(0.0004)	nd	(0.0008)
1279-TCDD	0.0015	(0.0004)	nd	(0.0008)
*1246-TCDD	nd	(0.0006)	nd	(0.0007)
1478-TCDD	nd	(0.0006)	nd	(0.0007)
1236-TCDD	nd	(0.0006)	nd	(0.0007)
1239-TCDD	nd	(0.0006)	nd	(0.0007)
*1249-TCDD	nd	(0.0007)	nd	(0.0007)
1368-TCDD	0.0048	(0.0007)	nd	(0.0007)
1379-TCDD	0.0017	(0.0007)	nd	(0.0007)
1378-TCDD	0.0043	(0.0007)	nd	(0.0007)
1234-TCDD	nd	(0.0007)	nd	(0.0007)
Total Other TCDD Isomers	0.0172		nd	
2378-TCDD	0.0030	(0.0007)	nd	(0.0008)
^{13}C•2378•TCDD Recovery:	81%		74%	

Explanatory Notes:

A. All TCDD isomers are determined by GC/MS using native 2378-TCDD as the primary reference standard.
B. All reported concentrations have been corrected for the observed ^{13}C•2378•TCDD internal standard recovery.
C. The limit of detection (values in parentheses) is defined as 2.5 x peak to valley noise in an adjacent portion of the mass chromatogram.
D. When observed signal is ≥25 x peak to valley noise, the limit of detection is not reported.

* Analytical methods don't allow for absolute confirmation that these two isomers are not reversed.

REMARKS BY PAUL F. OREFFICE, PRESIDENT AND CHIEF EXECUTIVE OFFICER
THE DOW CHEMICAL COMPANY

JUNE 1, 1983 PRESS CONFERENCE

SUBJECT: DOW ANNOUNCES SCIENTIFIC INITIATIVES
TO ADDRESS PUBLIC CONCERNS ABOUT DIOXIN

Good morning. All of you are well aware that the complex subject of dioxin has put Midland, Michigan, in the national spotlight. This has been the sort of notoriety we obviously didn't seek, but it has come anyway, and we are anxious to allay public concerns about dioxin in a meaningful and constructive manner.

In this age of instant communications, fame breeds fame, and the spotlight on dioxin in Midland has attracted a steady stream of reporters, camera crews, government officials and others. They've sought answers to questions about health effects, environmental impact and long-range implications, and we've worked hard to provide those answers. We've granted virtually every request for interviews from the news media. We've talked with state and federal government officials as well as to community leaders and others who want to better understand what is a very complicated issue. We've testified before state and federal legislative committees. We've opened our Michigan Division manufacturing plant to visits by those leaders and officials, and we're offering you the opportunity to tour our plant later today.

I am also convinced that Dow has done a responsible job of protecting its employees, protecting those who live in this community, and protecting people throughout the state from the potential hazards associated with any Dow industrial operation. And this includes exposure to dioxin.

Nonetheless, concerns exist, and criticisms exist. The list is long and is familiar to most of you. I have to tell you that bothers me -- a lot.

We believe we have been forthright and honest in responding to the many questions that have been asked of us. Sometimes we have been asked questions for which there are no absolute answers. For this we have been accused of equivocation or talking out of both sides of our mouth. When we respond unequivocally, we are accused of arrogance, or self-righteousness. I guess we can accept these accusations.

But what we cannot and will not accept is the level of anxiety and concern the publicity surrounding this issue has generated in this country, in this state, and for some in this community. To all these people we owe something very simple -- the right to live their lives without fear for their health, their children's health or the health of the generations that will come after them.

We believe -- I believe -- we have come up with an approach for addressing the understandably human concerns that people throughout the state and perhaps nationally are feeling about dioxin in Michigan.

So today I want to tell you about a comprehensive slate of scientific initiatives that Dow is launching.

This effort will seek, through sound science, to reassure those with concerns about dioxins. And it will aim at providing that reassurance with a sense of urgency. We intend to involve the concerted actions of state and federal government, of one or more universities, and, of course, of The Dow Chemical Company.

As you can imagine, this will be an expensive program. We're figuring on nearly $3 million of Dow money, and we're committed to see this program through. Now, I'd like to outline for you the six parts of the program we have in mind:

1. JOINT SOIL STUDY:

First, we will propose a joint and cooperative soil study with federal and state government agencies.

Following agreement on protocol, this study will involve: joint sampling inside our Midland plant, in the Midland community, and in other locations ... coding of those samples with split analysis ... allowances for independent laboratory validation ... joint announcement of results. We will offer our analytical services -- among the finest in the country. These results will expand the data base and encourage a meaningful interpretation of any potential health risks associated with minute quantities of dioxin in the soil.

Opening up our plant to this kind of sampling is very unusual for any industry and I think it should give you some idea of just how serious we are about this effort.

2. POINT SOURCE INVESTIGATION:

The second element of this program is an acceleration of our own continuing internal search for dioxin sources inside our plant. We will be looking at water ... at air ... at landfills. We will literally leave no stone unturned. We will be using the newest analytical techniques and capabilities available anywhere in the world. The ability to measure dioxin at parts-per-quadrillion levels will mean that Dow waste streams will be scrutinized with the most sensitive detection devices available today. We will use outside auditors to monitor our investigation. And we will ultimately share our findings with both the EPA and Michigan's Department of Natural Resources.

3. STUDY OF SOFT-TISSUE CANCER IN MIDLAND COUNTY:

Third, the Michigan Department of Public Health has been unable to establish any link between dioxin and soft tissue cancer mortality among white women in Midland County. We believe no such link exists. Nonetheless, we have offered the state health department our continued cooperation and financial assistance in expediting a case control study to further explore this question. We are doing so to assure that possible funding problems do not interfere with the orderly completion of that study.

4. EFFLUENT TECHNOLOGY STUDY:

The fourth step in our program is aimed at reducing dioxin in the Dow effluent stream -- even further reductions from the low parts per quadrillion now detectable in our wastewater discharge. We have established a grant to fund research at the University of Michigan to develop needed technology to get this job done. Municipal effluent will also be a focus of the study. We will publish the technology developed, and we will share the data with any interested party.

5. EXPANDED DOW ANALYTICAL CAPABILITY:

Fifth, we have authorized the expansion of our already formidable analytical capabilities. Additional scientists will be trained and more laboratory equipment will be installed to conduct these highly sophisticated analyses which will double Dow's capability to analyze for dioxin.

These first five measures seek to resolve concerns people may have about dioxin in our region. I'm sure you recognize that the dioxin issue is not limited to the Midland location or even the state of Michigan.

Concerns about the possible health implications of trace quantities of dioxin in the environment exist all across our country. Because we believe it will help answer those concerns, we support the EPA's proposed national dioxin study. We hope the government moves expeditiously to undertake the announced study, but recognize that a study of that magnitude may take several years to yield conclusions.

Our sixth initiative seeks to provide more timely reassurance to citizens in other states who may have fears about the health impact of trace dioxin exposure.

6. REVIEW OF HEALTH IMPACT:

We have already approached an independent and prestigious national scientific organization and invited them, with our financial support, to address this question: Do trace amounts of dioxin in the environment pose a health hazard to humans? That organization is considering our suggestion, and we expect to know soon if they will undertake this investigation.

Well, that's our six-point program. I'd like to finish my statement with a final thought.

Dow has consistently said that it believes the trace levels of dioxin found in this community and in other communities like Midland pose no significant threat to human health. We believe that with a great deal of conviction, and we believe the scientific evidence clearly supports our view. Moreover, some years ago, our research work led us to conclude that dioxins can be formed as a consequence of various combustion processes, and may have been with mankind a long time. Again, we are convinced that this conclusion is sound and that scientific evidence to support it continues to mount. In short, our perspectives and judgments about the dioxin controversy remain unchanged.

What has changed is that with all the publicity dioxin has received, the general public cannot be expected to take our word for it without corroboration. We understand that better than ever now, and that's the reason we have decided to take the initiatives announced here today, and why we invite and are encouraging third-party evaluation and verification of our own scientific conclusions.

I've covered a lot of ground ... and I imagine you may have a few questions about these new programs, so I'll turn the meeting back to Mr. McKennon.

# # #

FOR FURTHER INFORMATION
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DOW

Information from Dow

FOR FURTHER INFORMATION
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2020 Building
Midland, MI 48640
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FOR IMMEDIATE RELEASE

June 1, 1983

SUMMARY OF DIOXIN ISSUE
SCIENTIFIC INITIATIVES

INITIATIVE		RESOURCE DOLLAR COMMITMENT	APPROXIMATE TIME FRAME
I.	Cooperative soil study	$ 250,000	6 months
II.	Point source investigation	$1,000,000	6 months
III.	Soft tissue sarcoma study	$ 250,000	18 months
IV.	Effluent technology research	$ 250,000	18 months (interim results)
V.	Expanded Dow analytical capability	$ 750,000	Authorized expansion now underway
VI.	Independent health review	To be determined	
		$2,500,000	

DOW
Health & Environmental Information

For Further Information Contact:
R. W. (Bob) Charlton
(517) 636-9303

*DIOXIN AND HUMAN HEALTH

Executive Summary

The issue of dioxins in the environment and the possible human health effects of these compounds has been the subject of much speculation over the past decade.

This paper discusses scientific research and makes the following major points:

- The word "dioxin" refers to a family of 75 compounds of which the one called TCDD* is the most toxic based on animal tests. Dioxins can be produced as an unwanted contaminant of some manufacturing processes and through some combustion sources.
- An American Medical Association review of available research has concluded that there is no convincing support for allegations that TCDD causes cancer, birth defects or other reproductive difficulties in humans.
- Studies of some 30,000 people exposed to TCDD after an industrial accident in Seveso, Italy, found a chemically-induced acne that occurred in approximately 200 people and no persistent effects which could be verified. There was no excess of birth defects, abortions or deaths in the population.
- A number of studies of workers accidentally exposed to large amounts of TCDD as long as 30 years ago have identified cases of chloracne in some of those workers. However, no long-term health effects have been demonstrated among this worker group. The studies have looked for cancer, heart disease, liver damage and other ailments.
- The work of a Swedish scientist who purports to find a link between TCDD exposure and soft tissue sarcoma (a relatively rare cancer) is not consistent with other studies. This research is not supported by the bulk of studies of exposed industrial employees, herbicide applicators and others which show no excess of this type of cancer.

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*2,3,7,8-tetrachlorodibenzo-p-dioxin

- A study of 8,000 Dow employees in Midland, Michigan, where herbicides were produced, found their death rate to be 19 percent less than the general U.S. population. There was five percent less cancer than predicted.
- Investigations of herbicide applicators, forest workers and industrial workers and their wives found no link between TCDD exposure and birth defects.
- Studies of animals exposed to TCDD show a variety of adverse health effects that vary widely from species to species. In most studies, safe levels of dioxin exposure have been identified. Cancer occurred only at levels where animals were suffering from obvious TCDD poisoning.

A review of the scientific literature suggests that humans are less susceptible to TCDD than various animal species.

As is the case with other toxins, TCDD exposure should be carefully controlled. The scientific evidence to date does not warrant undue concern about individual exposure to trace amounts of TCDD currently measured in the environment. Government environmental guidelines currently provide for more than adequate margins of safety.

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*DIOXIN AND HUMAN HEALTH

During the past decade, considerable controversy has developed over the human health effects of exposure to TCDD, an unintentional contaminant from the production of some herbicides and antibacterial agents and a substance created by the process of combustion.

This controversy has been fueled by reports on the effects of Agent Orange exposure on returning Vietnam veterans, the Love Canal situation, the explosion of a 2,4,5-trichlorphenol plant in Seveso, Italy, and, most recently, the buy-out by the U.S. government of Times Beach, Missouri, a town contaminated with dioxin, (i.e., 2,3,7,8-tetrachlorodibenzo-p-dioxin [TCDD]).

During this time period, much speculation and misinformation regarding this issue have been generated, with resulting confusion and apprehension in the public mind. It is the purpose of this paper to state the facts regarding TCDD and human health and to place the issue in its proper perspective.

This paper will document the following key points:

- Certainly 2,3,7,8-TCDD is a potent and toxic compound that can cause a variety of ill health effects at relatively low doses in laboratory animals. We should be concerned with reducing any unreasonable risk of human TCDD exposure in our environment. Based on the preponderance of scientific studies, the trace environmental presence of TCDD does not pose a health hazard to people.

- There is a wealth of epidemiological data supporting the position that humans are far less susceptible to TCDD than several of the animal species which have been studied.

- The mere presence of TCDD in the environment (soil, water, fish, etc.) is not proof of contamination from industrial chemical sources.

- The scientific evidence does not demonstrate that TCDD exposure causes cancer in humans.

- There is no scientific evidence linking TCDD exposure in humans with a higher-than-normal rate of birth defects.

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*2,3,7,8-tetrachlorodibenzo-p-dioxin

What is Dioxin?

The term "dioxins" (or more scientifically, "chlorinated dibenzo-p-dioxins") refers to 75 similar, but different substances.[1]

Each of the 75 dioxins that has been studied has its own unique identity and toxicological properties.

On the basis of animal studies, 2,3,7,8,-tetrachlorodibenzo-p-dioxin (TCDD) is considered to be the most toxic of the dioxins, and it has been comprehensively examined for its toxicological effects. This report will generally address the health impact of TCDD exposure.

TCDD is a highly toxic compound that can cause a variety of ill health effects at relatively low doses in laboratory animals. We must be concerned with establishing safe levels of human TCDD exposure in our environment.

TCDD is not a commercial product. Pure TCDD is not commercially shipped in drums or railcars around the United States.

TCDD is formed as a trace contaminant in the synthesis of 2,4,5-trichlorophenol from tetrachlorobenzene. The herbicide 2,4,5-trichlorophenoxyacetic acid (2,4,5-T), other trichlorophenoxyacids, and the germicide hexachlorophene, all are synthesized from 2,4,5-trichlorophenol and may contain trace amounts of TCDD and other polychlorinated dioxins.2

Dow has not produced the herbicide 2,4,5-T in the United States since 1979 due to an Environmental Protection Agency (EPA) emergency suspension which restricted some applications of the product and reduced market demand. There are no manufacturers currently producing 2,4,5-T in the United States. A Dow joint venture company produces 2,4,5-T in New Zealand. Dow currently supplies 2,4,5-T from inventories for the rice and rangeland applications presently approved by EPA. The trace amount of TCDD present in Dow-inventoried 2,4,5-T is less than 10 parts per billion.

TCDD can also be produced as a by-product of combustion. Data indicate that chlorinated dioxins may arise from the combustion of most types of organic material, and suggest that chlorinated dioxins result from trace chemical reactions occurring in fire.[3]

Many chemical reactions occur during combustion at very low concentrations -- parts per billion and lower. With more advanced analytical capabilities, scientists have discovered numerous sources where various dioxins have been formed, including TCDD.

Some of these sources include refuse incinerators, wood-burning stoves, gasoline- and diesel-powered automobiles and trucks, fireplaces, charcoal grills and cigarettes. TCDD and the other dioxin compounds have been entering the atmosphere via airborne particulates from these various sources and settling on soil and in bodies of water.

There have been a number of industrial incidents throughout the world where people have been exposed to TCDD. Epidemiological studies have evaluated these incidents and all of the evidence so far tends to reduce the initial concern about the health effects of TCDD on humans. An overall look at the mounting data has been undertaken by the American Medical Association. These findings and conclusions are of interest and bear mention.

The American Medical Association Report

In 1981 the American Medical Association (AMA) published a technical report reviewing the medical evidence regarding the toxicity and long-term health effects of the TCDD contaminant in Agent Orange*.

The report's preface stated:

> "In spite of the voluminous data...there is still very little substantive evidence for many of the alleged claims that have been made against these compounds (dioxins). The most serious of these allegations assert that Agent Orange, or compounds of a like nature, have caused malignant tumors, spontaneous abortions and birth defects. Although data from studies on experimental animals tend to support some of these claims, it is not certain that the animal data are extrapolatable to man. No laboratory animal can fully substitute for man; we must, therefore, depend on the results of ongoing epidemiological studies on persons who are known to have been exposed."

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*(Agent Orange was a 50/50 herbicide mixture of 2,4,5-T and 2,4-D produced according to specifications set by the U.S. government for use as a defoliant in Vietnam to protect American troops from enemy ambush.)

A close look at the summary of the report gives a clearer insight into what the AMA's Advisory Panel on Toxic Substances found.

The AMA Panel reported that, in addition to the marked variations in the sensitivity and susceptibility of animal species to all toxic substances, there are significant differences between some of the toxic effects of TCDD in experimental animals and the human experience. People appear to be less sensitive to the health effects of TCDD than some of the animal species studied.

One of the more pronounced biological effects of heavy exposure to TCDD, as well as a number of other chlorinated aromatic compounds, is a tendency to cause chloracne in certain animals and humans, the AMA Panel reported. This particular skin condition is regarded as the clinical marker for TCDD over-exposure in people. The Panel noted that human systemic disorders from exposures to TCDD are unlikely to occur in the absence of chloracne. Such findings as impaired liver and kidney function, gastrointestinal irritation, muscle and nerve disorders, and depression and irritation of the central nervous system have been reported after exposure to large amounts of TCDD. However, these disorders have not been progressive, and they have disappeared with time, the AMA report stated. In short, if there is no chloracne, there are unlikely to be other persistent toxic effects from exposure to TCDD.

The AMA Panel also reported that other toxic effects of TCDD, when experimentally produced in test animals, appear as pathological changes in the liver, lymphoid and epithelial tissue.

TCDD is a powerful enzyme inducer. In addition to altering normal enzyme activity, it may potentiate or inhibit the action of other toxins.

The AMA report stated that TCDD may act as a promoter of carcinogenesis in some strains of rats and mice. For cancer to start, it must go through several distinct steps. The first stage, called initiation, is produced by a carcinogen (an initiator) and probably involves irreversible mutational changes. Subsequent growth and development of an actual cancer may require promotion, which may be the result of additional applications of a carcinogen, or of other, non-carcinogenic materials. Promotion may involve additional unknown processes which could aid the growth of the cancer or reduce resistance to the developing cancer.

TCDD is among the group of chemicals that may secondarily influence the formation of cancer by promotion. The carcinogenicity associated with TCDD in laboratory animals is typically accompanied by other signs of systemic toxicity in contrast to some other chemical carcinogens for which cancer is the only observable toxic effect.

TCDD has reportedly induced genetic changes in some forms of bacteria, but evaluations in rodents and humans do not indicate that these mutational changes will occur in higher animals, let alone people.

The AMA Panel made clear in its summary that the extensive information collected for more than 30 years provides no conclusive evidence that

2,4,5-T and/or TCDD are mutagenic, carcinogenic or teratogenic in humans, nor that they have caused reproductive difficulties in people.

Furthermore, the AMA report stated that 2,4,5-T undergoes relatively rapid decomposition in the soil. However, TCDD does persist in soil longer than 2,4,5-T, but, in general, the half-life of TCDD in soil may be no longer than one year. TCDD exposed to ultraviolet light is broken down rapidly when present as a thin film on plants, water and the surface of soil.[4]

Seveso

The most well-known and widely studied incident of community exposure to TCDD followed the July 10, 1976, explosion at the ICMESA trichlorophenol plant at Seveso, Italy. As a result of that accident, approximately seven square miles of the countryside were contaminated by chemicals, including TCDD, exposing as many as 30,000 people.[5,6] The heaviest contamination involved an area of 180 acres (Zone A), occupied by 736 people. TCDD was reportedly detected on soil at levels in excess of 5.5 parts per million (ppm).[7,5] In general, little effect was noted on plant life, but wild animals did die, particularly in Zone A (nearest the chemical plant). About four percent of the domestic animals in contaminated zones died, and virtually all of these were small animals.[5] Some of these deaths may haye been due to other chemicals released at the same time.

Chloracne, which has generally been regarded as the hallmark or sentinel sign of TCDD exposure[8], was observed in this population, although at generally low rates and primarily in children.[9,10,5,6] The highest incidence of chloracne reported was about 13-14 percent among elementary school children in Seveso, and this was generally mild and rapidly resolved in most affected people.[5,6,11] Other than chloracne (of which there were ultimately 100-200 cases), nausea, vomiting, itching and headache were the most commonly observed symptoms[6] readily attributable to the exposure which may have involved chemicals other than TCDD. Headache, stomach and intestinal upset were more commonly noted in individuals with chloracne.[9,6]

Bisanti[12] concluded that no "major event" had taken place with respect to birth defects, miscarriages (spontaneous abortions), births and deaths. While this seems to be the consensus, changes in birth defect reporting and in the reporting of "spontaneous" (sometimes "therapeutic") abortions have obscured any small changes which might have occurred.[13,5,6,14,11] Data on reproductive outcome are limited in number, but Reggiani[11] reports that examination of fetuses in 34 cases of medically-induced abortion revealed no evidence of injury attributable to TCDD. Pregnancy outcome in the years following 1976 appears to be comparable with Western experience.[6]

Of particular interest is the fact that no birth defects were observed during 1977 among the 70 births in Zones A and B. Only those pregnancies coming to term after January 1977 would have been relevant, i.e., those in which July 1976 maternal exposure would have taken place during the critical period for the developing fetus.

Many factors are known to cause birth defects in humans, which occur in three to six percent of live births: viral infections, genetic predisposition, smoking, alcohol, and even medications, including excess quantities of certain vitamins.

Epidemiological Studies

In recent years a number of investigations have been conducted concerning the human health effects associated with exposures to TCDD.

The following brief review of the human exposure experience with TCDD and the epidemiological studies of those people is taken from a recent report by the Advisory Committee on Pesticides, which is charged with making recommendations concerning the safety and safe use of pesticides in the United Kingdom.

- Monsanto's plant at Nitro, West Virginia: 121 workers were followed up for 30 years after exposure to TCDD. No apparent excess in total mortality or in deaths from cancer or diseases of the circulatory system was observed.[15]
- Coalite plant (1968) in the United Kingdom: Chloracne was initially seen in 79 workers and some had initial abnormalities in the liver but these returned to normal limits within 10 days. No clinically recognizable disease has been demonstrated. There is no evidence of liver or cardiovascular disease.[15]

- Dow Chemical Company workers exposed to 2,4,5-T: No adverse effects have been noted in an epidemiological study in these workers (mortality was actually less than expected).[15]
- Vietnam: Exposure to Agent Orange is blamed for a host of illnesses. The U.S. Veterans Administration found that no cause-effect relationship was established between TCDD exposure and alleged medical complications.[15]
- Finnish railroad workers using 2,4,5-T and other phenoxyacetic acid herbicides in forestry and on roads and railways: 1,960 men were studied and no increased mortality from cancer was demonstrated. There were no deaths from cancer in forestry workers although six deaths would have been statistically predicted.[15].

Soft Tissue Sarcoma

The most persistent hypothesis deals with the possible causal association between TCDD and soft tissue sarcomas. This hypothesis is derived from the epidemiological work done by Dr. Hardell and his associates in Sweden.[16]

Soft tissue sarcoma is a generic term for a group of lesions that include more than 100 different types of tumors.[17] These tumors are relatively rare; thus few pathologists have been able to achieve a high degree of consistency in their diagnosis.[18] Most experts believe that if TCDD were acting as a carcinogen it would cause an increase in one type of soft tissue sarcoma, but would be unlikely to raise the risk all across the board. One of the reasons vinyl chloride is accepted as a human carcinogen is the specific way it acts. At high levels, it produces a single type of cancer: angiosarcoma of the liver.

The question which arises is: If there is a common exposure link between various reports of soft tissue sarcomas in occupational groups, is TCDD the link?

The exposure documentation differs from study to study. In some, based on detailed technical knowledge of the chemical process, analyses of reaction contaminants, and clinical evidence of excessive group exposure (such as chloracne), there is evidence that TCDD is at least one of the common exposure links. In other reports, the evidence is more presumptive, and in some cases it is totally lacking.

Epidemiologists from Dow Chemical and Monsanto have reported on the soft tissue sarcoma cases occurring in their occupational groups presumably exposed to high levels of 2,3,7,8-TCDD.[19,20,21]

In 1964, a group of Dow trichlorophenol production workers experienced an outbreak of chloracne. Sixty-one workers were identified as being involved with the trichlorophenol process. Forty-nine of these workers developed a rash diagnosed as chloracne. Epidemiologists followed up on the status of all 61 men in 1978, 14 years after the incident. Statistically, 7.8 deaths would have been expected in this group, but only four had occurred. Among the causes of death, one was from cardiovascular disease when 3.8 would have been expected. Cancer was identified as the cause of three deaths when 1.6 were expected. None of these findings represent a statistically significant deviation from the expected experience[20]. One of the cancer deaths in the Dow group was due to soft tissue sarcoma.

In the 1978 Monsanto study, no link between exposure to TCDD and excess deaths due to cancer or other causes was found among 121 current and former workers employed at a plant in Nitro, West Virginia. The employees who participated in the study included workers who developed chloracne as a result of over-exposure to TCDD in a manufacturing accident in 1949.

Among the Monsanto workers studied, 32 deaths were reported versus 46 which would be expected. Cancer accounted for nine deaths among the Monsanto group compared with slightly more than nine deaths expected. One of these cancer deaths was attributed to soft tissue sarcoma.

In a group of Dow 2,4,5-T employees (none of whom had chloracne)[22] there have been no cases of soft tissue sarcoma.

At Dow, the mortality experience of 204 persons exposed to 2,4,5-T during its manufacture from 1950 to 1971 was studied through 1978. No adverse effects were observed with respect to occupational exposure to either 2,4,5-T or its feedstock, 2,4,5-trichlorophenol. Mortality of the studied workers was favorable compared to that of U.S. white males.

There have been no cases of soft tissue sarcoma reported in a BASF worker group, many of whom experienced severe chloracne. Seventy-four members of the BASF group were exposed to TCDD during a 1953 accident in a trichlorophenol production unit or during cleanup and repair following the accident. Exposures were heavy. Twenty-seven years after the accident a mortality study of those exposed to TCDD in the accident was undertaken. Overall mortality did not differ in this group from the rate expected in three external reference populations or from that observed in two internal comparison groups.

Dow is cooperating with the National Institute for Occupational Safety and Health (NIOSH) to prepare a study of more than 4,000 industrial workers potentially exposed to dioxins.

Swedish Epidemiological Studies

Dr. Hardell's work, which has lead to the question about soft tissue sarcomas, uses a different methodology than in the foregoing studies -- the case control approach -- and reports on different patterns and levels of exposure.[16,24] In his first study, he reported a five- to six-fold increased risk of soft tissue sarcomas for those presumably exposed to phenoxyacetic acids, predominantly 2,4,5-T, and chlorophenols ("presumably" because the exposure information was subjectively reported by the study participants and/or next of kin). Objective records were incomplete and were difficult to interpret. In the second study, he also estimated the risk associated with exposure to phenoxyacetic acids not contaminated with TCDD and found the same magnitude of risk.

Some epidemiologists reviewing the information find this confusing. The justification for combining chlorophenols and 2,4,5-T was the presumption of a common contaminant, TCDD.[24] If that were the case, increased risk would not be expected for the phenoxyacetic acids without this contaminant.

In both of his studies, Dr. Hardell first administered mail questionnaires and then followed up with telephone interviews on a selected subset of subjects. While the questionnaire was designed with the idea of masking the intent of the investigation, the telephone inquiry specifically focused on the exposures of pertinent interest: phenoxyacetic acids and chlorophenols.

Interestingly, in his second study, Dr. Hardell reported the frequency of the various exposures among both cases and controls and most of the risk estimates were elevated. The risk from only one out of 15 chemicals, sodium chlorate, was not elevated. Nicotine had a high risk. Unfortunately, the risk estimates derived from the questionnaire alone are not known, nor is it known what the risk estimates would have been for other agents, if they had been probed in the same depth as were the phenoxyacetic acids and chlorophenols.

There are a number of other concerns relating to Hardell's work. The accuracy with which exposure to the chemicals is determined is of vital importance, and the memory recall techniques Dr. Hardell used are subject to error. Workers are unlikely to remember with accuracy the chemicals they used some years in the past. It is also extremely difficult to estimate the extent or duration of the exposures. Furthermore, the identification and classification of the various soft tissue sarcomas have not been consistent. The diversity of tumors is particularly difficult to explain. If all the tumors had been of a single type, the data would be much more convincing.

Furthermore, research currently underway does not support Hardell's hypothesis concerning soft tissue sarcoma:

- The U.K. Government Advisory Committee on Pesticides noted in February 1983: "It is our view that the procedures used for establishing the Swedish study groups, and some aspects of the collection of the exposure data, were not reliable."
- Smith and associates[25] are conducting a case-control study in New Zealand. Herbicide application is a registered profession in New Zealand, and phenoxyacetic acids have been used in bulk since the late 1940s. In a preliminary report presented at the 1982 International Symposium on Chlorinated Dioxins and Related Compounds, Smith noted he was unable to establish an association between the use of phenoxyacetic acids and soft tissue sarcoma. In fact, not one of the soft tissue sarcoma patients had ever worked as a licensed phenoxyacetic acid herbicide applicator.
- Milham[26] explored this issue in the state of Washington using death certificates. While there has been considerable exposure over the years to phenoxyacetic acids and chlorophenols in Washington state, occupations related to their use did not show consistent patterns of death due to soft tissue sarcomas. Surprisingly, the two occupations with the highest proportional mortality ratios were marine engineers and bankers.
- Among the deaths in the U.S. Air Force "Ranch Hand" Study, none were due to soft tissue sarcomas.[27]
- Riihimaki studied 1,960 Finnish herbicide applicators and found no difference in death rate from any natural cause, including cancer, compared with the total Finnish male population. There were no soft tissue sarcomas reported in this group of workers.[28]
- The Michigan Department of Public Health (MDPH) is investigating the possible relationship between dioxin and a small number of soft and connective tissue cancer deaths among women in Midland County (where Dow has facilities).[29] In a recent report (May 1983) MDPH

did not identify a specific association between any environmental factor and the reported increase of soft tissue cancer in the county. While overall age-adjusted cancer mortality rates in Midland County were below the state of Michigan average, soft and connective tissue cancers among white females in the county were elevated. As part of the initial study, MDPH reviewed data for 28 other U.S. counties in which TCDD or other dioxins were likely produced as a chemical manufacturing contaminant. They found no increase of soft tissue cancer in these counties versus counties that did not have industrial manufacturing sources suspected of generating such dioxins.

- Various animal species did not develop soft tissue sarcomas when fed TCDD during laboratory experiments.

Additional research is underway in the United States and elsewhere. The results of these studies should offer a better perspective on this issue. But right now, the preponderance of evidence does not demonstrate a link between TCDD exposure and soft tissue sarcomas.

The Dow Mortality Study

In 1976 a research study was published that summarized the mortality experience of over 8,000 men employed by The Dow Chemical Company. The population of interest was defined based on a March 1, 1954, employee census of the Midland, Michigan, manufacturing location of the Company.[30]

The study originally developed background mortality data on the Dow worker population so that findings obtained from smaller groups directed at more specific questions, (e.g. questions regarding particular chemical exposures or processes), could be placed in perspective. The observation period for mortality follow-up was 1954 through 1972, and comparisons were made to the mortality experience of the corresponding United States white male population. At that time, mortality among Dow employees was found to compare favorably with that of the general U.S. population.

The objectives of the most recent update of this group of 8,181 employees were to extend the observation period through 1978, and to include comparisons with a community-based group of employed men not engaged in chemical manufacturing activities. In addition, the effects of cigarette smoking on mortality were investigated.

The Dow group consisted of personnel from research departments, the corporate headquarters, and a major manufacturing division of the Company. It has been estimated that as many as 500 distinct chemical processes ranging from small batch operations to large continuous and highly-automated production units have been onstream at the Midland manufacturing site, including production of trichlorophenol and related products.[31]

For the most part, the men in the study represent long-term Company employees. Some were hired prior to the 1940s.

Cause of death was obtained from death certificates for all but nine of the 1,932 deceased members of the study population, Overall mortality in the Dow group was 19 percent less than that expected for the corresponding United States population. Expressed in another way, a Dow worker of age 25 in 1972 could expect to live 2.2 years longer than a non-Dow worker of the same age.

There were no statistical findings of excess mortality among Dow employees for any cause of death category. For total malignant neoplasms, there were five percent fewer deaths observed than expected based on the United States white male population. Significantly fewer deaths were observed than were expected for all categories. Presumably, if low-level TCDD exposure caused a variety of increased illnesses, the opposite from what is stated above would have been found.

Comparing the Dow workers with a comparable employee population in Michigan, the overall mortality risk was about 10 percent lower in the Dow group than the corresponding non-Dow group.[32]

Birth Defects

Concerns that TCDD may cause birth defects are not substantiated by epidemiological science. A brief review of some areas of concern and the corresponding results, and a more specific look at the Dow situation in Midland, Michigan, are presented:

- Aerial spraying of 2,4,5-T in Oregon: Claims of a link between incidence of miscarriages and 2,4,5-T herbicide could not be established when all the data were available.[15]

- A six-year study of agriculture and forestry workers in Hungary exposed to 2,4,5-T: Data do not suggest that there has been any significant increase of birth defects.[15]
- New Zealand workers exposed to 2,4,5-T: An alleged abnormally high incidence of neural tube defects (such as spina bifida) were chance occurrences, and there is "a very high assurance of safety in normal use" of 2,4,5-T.[15]
- Australian worker exposure to 2,4-D and 2,4,5-T: Claims of high incidence of birth defects were investigated, and available information revealed no evidence that the birth defects were caused by exposure to these two compounds.[15]
- Facial cleft defects in Arkansas: Study of exposure to 2,4,5-T from 1948-74 reveals these defects to have no association with 2,4,5-T.[15]

About five years ago it was reported that the birth defect rates in Midland County (Michigan) were three times above those for the state of Michigan. At that time, the Michigan Department of Public Health (MDPH) examined this issue. It found an increase had occurred between 1971 and 1974 due to additional reporting of minor congenital malformations. Before 1971 and after 1974, the birth defect rates in Midland County were either at or below state rates. If widespread chemical contamination of the environment was responsible for birth defects, the rates should have gone up and stayed up. They did not. The changes may have been due to reporting techniques, not additional cases of birth defects.

It is very important to note that the numbers of county births and birth defects were small, and thus, rates calculated from them tended to be more variable from year to year than the comparable rates for the entire state. The MDPH recently announced (May 1983) an updated report which concludes that the birth defect elevations noted in the early 1970s were not unique and that no additional studies are warranted at this time.[57]

In 1982 Dow scientists published a report of a survey of reproductive events among 370 wives of Dow Michigan Division employees exposed to dioxins.[33] They analyzed the associations between exposure and spontaneous abortion (miscarriage), stillbirths, infant deaths, and several categories of congenital malformations before and after controlling for multiple confounders (i.e., sources of error or confusion) independently and in various combinations. They did trend analysis to determine if duration of paternal exposure was related to adverse pregnancy outcome. There were no associations between any exposure and adverse pregnancy outcomes. These findings have recently been confirmed in another study conducted by Australian scientists[34] who examined the impact on birth rates involving Vietnam veterans potentially exposed to Agent Orange.

The Toxicity of TCDD in Animal Species

There are wide variations in how different animal species are affected by TCDD. For example, the single oral dose LD_{50} (the amount that it would take to kill 50 percent of the test animals) in guinea pigs is 0.6-2.0 ug/kg (micrograms per kilogram or every 2.2 pounds of body weight [a microgram is one millionth of a gram; a kilogram is 1,000 grams, or 2.2 pounds]).[35,36] In hamsters, however, TCDD is much less toxic, with an oral LD_{50} of 1157-5051 ug/kg.[37,38]

Therefore, the guinea pig is approximately 5,000 times more sensitive than the hamster, although both species are closely related biologically. The direct relevance of any single animal experiment to humans must be evaluated with respect to all other available data.

In acute and subchronic studies, liver toxicity is a prominent component of TCDD toxicity in rats, mice and rabbits, but not in monkeys, where effects on the bone marrow and epithelial tissue are more prominent.

Thymic atrophy in early toxicity studies suggested that TCDD might decrease the immune response. In laboratory animals, scientists can induce immunotoxic effects with high doses of TCDD. However, as the Seveso incident shows, these effects have not been demonstrated in exposed humans.[39,40]

Teratogenicity/Animal Species

Of the various toxic responses of animals to TCDD, the potential for teratogenicity (birth defects) has perhaps received the most attention. Teratogenic effects resulting from TCDD have been realized only in mice, which show an increased frequency of cleft palate, along with an abnormality of the central collection system of the kidney. It is well known that many factors can cause birth defects in mice, including the stress of being transported by air during pregnancy, or being deprived of drinking water overnight. In both rats and mice, dose levels of TCDD have been identified at which these effects do not occur.

In rats, TCDD does not cause a teratogenic effect but sufficiently high doses can cause embryo- and fetotoxicity.

Many of the studies with TCDD in monkeys have been conducted at the University of Wisconsin. In experiments where the high dose level of about 0.011 ug/kg/day TCDD in the diet was given to the monkeys for up to 9.3 months, there were substantial toxic effects.[41,42] A preliminary abstract of a follow-up study[43] showed that monkeys given diets containing approximately 0.0017 ug/kg/day of TCDD had only slight toxicity. There are studies currently in progress at the University of Wisconsin at lower doses.

In a three-generation reproduction study[44] of rats at high-, medium-, and low-dose levels of TCDD in the diet, high doses caused decreased fertility and neonatal survival. The intermediate dose level caused decreased fertility and other effects in the first two generations, but not in the third. At the low-dose level, there was no impairment of reproductive capacity through the three consecutive generations, indicating that 0.001 ug/kg/day was a no-adverse-effect level over multiple generations.

Mutagenicity/Animal Species

A number of mutagenic studies have been conducted with TCDD. The majority of the tests have been negative or uninterpretable. Only two of the tests were positive in one strain of Salmonella bacteria, showing that there is low possibility for mutagenesis with TCDD in bacteria.

In studies[40,45,46,47,48,49,50,51] with rats or human cells, there is little indication that TCDD elicits a mutagenic response.

Thus, while a few positive or questionable mutagenic responses have been observed in certain plant or microbial test systems, there appear to be no definitive correlates of mutagenicity in higher animals or humans.

Carcinogenicity/Animal Species

Carcinogenic studies following ingestion of TCDD have been conducted in rats and mice.[52,53,54] Review of these data indicates good correlation of the results in rats and mice, with a carcinogenic response associated only with lifetime ingestion of higher dose levels that also induce other toxicity. The liver was the primary target for cancer in both rats and mice. No cancer response occurred at dose levels of 0.001-0.0014 ug/kg/day in the rats and 0.001-0.03 ug/kg/day in mice.

TCDD does cause cancer in animals. However, it is only at very high dose levels -- dose levels that are higher than those that elicit other kinds of toxicity. Cancer induced by exposure to TCDD would be preceded by substantial signs of toxicity. This toxicity (which is reversible when exposure stops) would act as a sentinel, or warning at dose levels below those that might cause cancer.

Environmental Hazard Evaluation

Soil

Potential human exposure to TCDD from environmental contamination concerns many people. The following factors should be considered when evaluating potential human health hazards due to TCDD in soil:

- TCDD is tenaciously bound by soils and other materials (carbon, charcoal), and studies have shown that plants grown in soils containing TCDD do not accumulate or translocate the material.

- The amount of material absorbed depends on contact with the skin, or ingestion.

- Soil binding of TCDD reduces the amount that can be absorbed through the skin or internally from ingestion.

- Animal studies show that only a small amount of TCDD is absorbed from contaminated soil. In animal studies, when such soil contained about 500 parts per billion (ppb) ppb TCDD and when the soil was held in contact with skin for 24 hours (covered with aluminum foil), about 1/1000 of the TCDD in soil was absorbed.

- Estimates of absorption from the Seveso incident suggest that people would be expected to absorb about 1/2000 of the average amount of material present in 1 square meter (approximately 1.2 square yards) of their environment each day. If one uses the laboratory or Seveso data, one can estimate that 100-1000 ppb TCDD in soil could result in human absorption of as much as a dose equivalent to that which produced no effect when fed to laboratory rats for a lifetime. If one assumes that soil is eaten in significant amounts by children, the permissible level is less, perhaps 10 ppb.

Based on the assumptions and calculations presented here, (particularly those based on the work of Dr. Kingsley Stevens),[56] it appears that general environmental soil contamination in the range of low parts per billion would not pose a health hazard to the general population, including the unborn, children, pregnant women or the old and infirm. For the general population, excluding children with intimate soil contact or those who ingest soil, a level of 100 ppb would still pose no hazard. In occupational settings, where workers are protected by standard industrial hygiene practices, higher levels of contamination would not be accompanied by greater exposure or hazard.

Dioxin and Fish

Rats consuming a diet containing 22 parts per trillion (ppt) ppt TCDD (1 nanogram TCDD/kg of body weight per day) for a lifetime showed no adverse health effects due to TCDD. Rats consume about 10-20 percent of their body weight in food each day, while people daily consume about 2-3 percent of their body weight. Thus, for a given TCDD concentration, rats will ingest more of the compound than people. A person eating about 2-3 pounds of food per day uniformly contaminated with 25 ppt TCDD would ingest about 0.5 nanogram/kg body weight/day or about one-half the dose (weight of TCDD per unit of body weight) shown to produce no adverse health effects when fed to rats for a lifetime. Again, this is true because people eat less food in proportion to their body weight compared to laboratory rats.

The dose received by eating contaminated fish is much less. Most people in the United States (99 percent according to U.S. government figures) eat less than 0.6 pound of fish per week. Nine out of ten people in the United States eat less than 0.3 pound of fish per week, while the "average" person eats still less. Since fish is such a small part of the American diet, 99 percent of the American public would receive less than 1/70 of the amount of TCDD shown to produce no effect in laboratory rats fed TCDD daily for their lifetimes, if those people ate fish containing 25 ppt of TCDD. Or said another way, a person could eat nearly one ton of fish per year containing 25 ppt of TCDD and not exceed the no-effect level established by laboratory animal experiments.

The fish consumption guideline of 25 ppt established by the Food and Drug Administration assures an adequate margin of safety to protect people from overexposure to TCDD.[55]

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EXHIBIT G

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SURVEY OF REPRODUCTIVE EVENTS OF WIVES OF EMPLOYEES EXPOSED TO CHLORINATED DIOXINS

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To determine whether paternal exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) or other polychlorinated dioxins might be associated with adverse pregnancy outcomes, an interviewer-administered questionnaire survey was conducted among wives of Dow Michigan Division employees in the Midland, Michigan, area who had been potentially exposed to dioxins. A control group consisted of wives of employees who had no dioxins exposure and whose hire dates were comparable to those of the men in the exposed group. A total of 737 conceptions, which resulted in 637 live births and 100 stillbirths and spontaneous abortions, were identified as having paternal exposure; 2031 conceptions, resulting in 1785 live births and 246 stillbirths and spontaneous abortions, were identified as having no paternal exposure to any isomer of dioxin. Odds ratios were calculated for dependent variables consisting of spontaneous abortions, stillbirths, infant deaths and several categories of congenital malformations. Trend analysis was performed for duration-of-paternal-exposure of 12 months or less, or more than 12 months. Overall, no statistically significant associations were found between any exposure and pregnancy outcome, either before or after stratification by pertinent sets of up to nine covariables.

abortion; congenital defects; dioxins; questionnaires; stillbirth; tetrachlorodibenzodioxin

This paper describes the results of an interviewer-administered questionnaire survey conducted among women whose husbands were employees of the Midland, Michigan Division of Dow Chemical U.S.A. The purpose of the survey was to compare the proportion of adverse outcomes between pregnancies associated with potential paternal exposures to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD), or other polychlorinated dioxins, and pregnancies with no known exposures to these chemicals.

Polychlorinated dibenzodioxins, hereaf-

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Abbreviations: FORTRAN, Formula translator, a computer programming language; ICD-8, International Classification of Diseases, Eighth Revision; PL1, Program Language 1, a computer programming language; SAS, Statistical Analysis System, a computer software system; TCDD, 2,3,7,8-tetrachlorodibenzo-p-dioxin; 2,4,5-T, 2,4,5-trichlorophenoxyacetic acid.

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ter referred to as dioxins, may be formed during combustion of carbonaceous fuels or during production of chlorinated phenols (1). Of all the isomers of dioxins, TCDD, a low level contaminant of 2,4,5-trichlorophenol and its byproducts, is considered the most toxic, with an acute single oral LD_{50} in the low μg/kg range for some laboratory animals (2).

Numerous bacterial or plant test systems have been used to evaluate potential mutagenicity of the dioxins. Hussain et al. (3) found evidence of frameshift mutations with *Salmonella typhimurium*, strain TA 1532, but others have reported doubtful mutagenicity for strains TA 1531 and TA 1534, and non-mutagenicity for strains G-4 and TA 1530 (4).

Mammalian *in vivo* mutagenesis tests have also been performed. Green and Moreland (5) concluded TCDD had no potential for producing chromosomal aberrations in the bone marrow of rats; however, in a subsequent study at higher levels, Green et al. (6) observed an increase which they regarded as weakly positive. Khera and Ruddick (7) exposed male rats to 4, 8 or 12 μg/kg/day of TCDD for seven consecutive days and then conducted sequential mating trials. Though some levels of the compound caused dose-related toxicity and mortality, there were no dominant lethal mutations noted during the post-treatment period.

A three-generation reproduction study of rats given TCDD, including crossmating with younger untreated animals, indicated adverse reproductive events associated with maternal exposures, but not paternal exposures (8). The latter was true even at the highest dose level, 0.1 μg TCDD/kg/day (8). Very recently, experiments involving daily oral administration of up to 2.4 μg/kg TCDD to male mice were reported to have no effect on reproduction or fertility (9).

There have been a series of observational studies of humans related to the mutagenicity or teratogenicity of TCDD or other dioxins. The National Academy of Sciences, commissioned to study the effects of herbicides in South Vietnam, found no conclusive evidence of an association between exposure to herbicides and birth defects in humans (10). Field and Kerr (11) purported a "linear correlation" of neural tube defects and increased use in Australia of the herbicide 2,4,5-trichlorophenoxyacetic acid (2,4,5-T), an herbicide with low levels of TCDD. A similar graph was constructed by Thomas (12) for Hungary where 2,4,5-T usage increased dramatically between 1970 and 1976, but the incidence of stillbirths and congenital malformations remained stable or decreased.

There have been claims of human dioxin-related congenital malformations among offspring of United States and Vietnamese veterans of the Vietnam conflict who were exposed to aerial herbicides spraying (13, 14) and of increased spontaneous abortions among women residing in or near areas of Oregon sprayed with 2,4,5-T (15, 16). Neither of these allegations has been substantiated epidemiologically and the Oregon abortion data, when subjected to critical review, were found not to support the conclusion of an association with herbicide usage (17–19).

Surveillance data on humans have been available following proven contamination of a fairly extensive area with TCDD after a pressure vessel release at a trichlorophenol plant in Seveso, Italy in 1976 (20). Continued monitoring of the population in this area has shown no correlation between spontaneous abortion rates and exposure calculated on the basis of proximity to the factory (21). Although there have been fluctuations in reported congenital malformation rates and spontaneous abortion rates in Seveso during 1976 to 1977, these were reportedly below the Italian national average and there was no pattern consistent with proximity to the site of the release (21). Negative results of cytogenetic evaluations of maternal peripheral blood cells and fetal tissues from TCDD-exposed humans at Seveso have been reported (22–24). The actual degree of exposure to TCDD of husbands and wives in Seveso is unknown, but was sufficient to cause chloracne in 164 children and 23 adults (20).

Dow Chemical U.S.A. has conducted a series of epidemiologic studies of employees potentially exposed to dioxins (25, 26). This survey of reproductive outcomes associated with paternal exposures to dioxins was part of the surveillance program.

MATERIALS AND METHODS

Source of exposed and control populations

Identification of wives whose husbands had been potentially exposed to dioxins was accomplished via company records. Using annual census lists maintained by the Personnel Department of The Dow Chemical Company, Michigan Division, it was possible to identify employees who had worked in any one of seven buildings associated with chlorophenol processes and hence who were potentially exposed to dioxins. Individual work histories were examined and an employee was considered exposed if he had been assigned for at least one month to specific jobs in the chlorophenol processes between January 1939 and December 1975. By these criteria, a total of 930 male employees with potential dioxins exposures were identified.

An equal number of controls was selected from male employees who, according to work histories, had worked for the company for one month or more, had no job assignments in the potential exposure areas, and closely matched exposed employees by date of hire. Tracing of exposed and control employees was by company records for active employees and retirees receiving benefits. Follow-up of those who had left employment before January 1, 1976, was attempted by submitting names and birth dates to the Michigan Drivers' License Bureau, by searching local telephone directories, by contacting relatives mentioned on work histories, and by submission of names and Social Security numbers to the Social Security Administration. Addresses were thus obtained on all but 69 (3.7 per cent) of the 1860 men. Follow-up was limited to those who lived in Midland or adjacent counties (table 1). Of 930 men in the exposed group, 586 had wives potentially available for interview and 370 agreed to participate. Among the control group, 559 wives were potentially available and 345 were interviewed.

Estimation of exposures

One way dioxins are produced is as byproducts of the manufacture of chlorophenols. Under alkaline conditions, at elevated temperatures and high pressures, bimolecular condensation of chlorophenates may occur. Although theoretically 75 possible polychlorinated dioxins could be formed by condensation of chlorophenols, symmetrically substituted isomers with even numbers of chlorine atoms, including TCDD, were more likely to be formed in the Dow manufacturing processes. Potential dioxins exposures at the Michigan plant existed mainly in the areas which produced or used 2,4,5-trichlorophenol and pentachlorophenol.

Production of pentachlorophenol started in 1939 and 2,4,5-trichlorophenol production started in 1946. Pentachlorophenol was produced by reacting phenol with chlorine, followed by distillation, further chlorination, or treatment with sodium hydroxide, depending on the desired end product. Dioxins associated with these reactions were mostly the higher isomers (hexa-, hepta- and octa-chlorodibenzo-p-dioxins). In 2,4,5-trichlorophenol production, tetrachlorobenzine was hydrolyzed with sodium hydroxide to produce sodium trichlorophenate; TCDD was formed as a byproduct in this reaction and was con-

TABLE 1

Selection and study participation frequencies among families with husbands never exposed or potentially exposed to dioxins during production operations at the Dow Chemical Company Michigan Division Site, Midland, Michigan, 1939–1975

Status	Exposed group	Unexposed group
Male employees identified as being unexposed or potentially exposed to dioxins	930	930
Employee deceased	125	119*
Employee widower or single	97	84
Family residing outside area	95	126
No address available (presumed living)	27	42
Wife eligible for interview	586	559
No response	18	19
Refused	198	194
Interviewed	370	345*

* It was discovered during the interviews that one woman was widowed, and two others thought to have unexposed husbands were misclassified. Interviews from the two latter were not used, so only 345 of the control interviews were analyzed.

centrated mainly within a caustic insoluble oil layer. The sodium trichlorophenate then was acidified and the resulting 2,4,5-trichlorophenol distilled. In late 1963, a change was made in this process and shortly thereafter a number of employees contracted chloracne. Operations were then modified to minimize exposures. In 1966, 2,4,5-trichlorophenol production was transferred to a new building where new equipment and controls, including automated oil layer dumping, greatly reduced the potential for exposures.

Estimation of exposures was made by an industrial hygienist who was familiar with the processes described above. Based on his experience, information provided by production personnel and surface contamination data, the industrial hygienist estimated exposure potential of jobs within each building in the 2,4,5-trichlorophenol or pentachlorophenol processes. Surface contamination data consisted of wipe tests analyzed by rabbit ear bioassay prior to 1964 and by gas chromatography and mass spectroscopy since 1964. It was presumed that most exposures would have been by skin contact.

Each job was assigned an exposure potential on a scale of low to high for TCDD, for all other dioxins, or for mixed exposures. Jobs involving drying, grinding and packaging of pentachlorophenol and its salt were considered to have had exposure to dioxins other than TCDD. Jobs categorized as low TCDD exposure included 2,4,5-trichlorophenol packers and most 2,4,5-trichlorophenol production operators. The category of moderate TCDD exposures was assigned to mechanics and janitors and to certain operators in 2,4,5-trichlorophenol production and to still operators in the 2,4,5-trichlorophenol distillation area. High potential TCDD exposure was assigned to all jobs involved in the 2,4,5-trichlorophenol process area in late 1963 through 1964, which was when the cases of chloracne occurred (25, 26).

Collection and analysis of data

After cooperation of the local labor union had been obtained, a letter explaining the purpose of the study and requesting a personal interview was mailed to the residence of each living exposed and control population member residing in Midland or adjacent counties. Appointments were made with those women willing to be interviewed. If an employee was a widower or single, or if the response indicated the wife did not wish to be interviewed, no further action was taken. However, if there was no response after several days, a phone call was made to re-explain the intent of the study and to encourage participation. Arrangements were made with those who agreed to be interviewed. No deliberate attempt was made to determine why women did not wish to be interviewed, but unsolicited reasons included divorce, death of spouse, or no pregnancies.

Interviews were conducted in the home by one of the three trained nurse-interviewers. To minimize driving time, appointments were arranged by geographic clusters, rather than by assignment to exposed or control group. Interviewers did not know whether they were interviewing wives of exposed or control employees. At the time of the interview, the intent of the study was re-explained; each woman was advised regarding confidentiality of the information and was asked to sign an informed consent. The interview process normally took less than one-half hour. A five-page questionnaire was used, and answers were recorded in writing on a separate form for each interviewee. Questions were designed to elicit demographic data, marital and family histories, and information considered relevant to pregnancy outcomes. Responses concerning individual pregnancies were used to define and categorize the covariables described below. In addition to questions regarding illnesses associated with pregnancy and the puerperium, there were open-ended questions about unusual events during or immediately after each pregnancy.

Answers were coded and computerized. Responses dealing with health defects, congenital malformations and infant deaths were coded by the Eighth Revision of the *International Classification of Diseases* (ICD-8) (27). Each positive response regarding congenital malformations was coded if the mother stated the condition was diagnosed prior to one year after birth or if the mother was unclear as to time of diagnosis. Conditions identified after the first birthday were reviewed by two physicians. If either physician, blinded as to mother's group, determined the defect could be diagnosed during the first year of life, the condition was so coded. Since these procedures were weighted toward identifying abnormalities, the resulting data could not be meaningfully compared to state or national statistics.

Keypunched data were stored and analyzed on an IBM 370/158 system, with FORTRAN, PL1 and SAS software. For statistical analyses, continuous variables were transformed to categorical; the transformed or generated variables used in analyses are described below in accordance with whether they were considered dependent variables, independent variables or covariables.

Although some complementary analyses were performed using the mother as the observational unit, for the main purposes of this study, the individual conceptus or product of conception was the observational unit, taken as independent of other conceptuses of the same pregnancy or other pregnancies of the same or different women. Effect of exposure to dioxins was conservatively considered as an irreparable event; that is, any exposure of a male employee any time prior to the estimated date of each conception attributed to him was investigated as an independent variable with potential effects on the pregnancy outcome. Conception dates were estimated from the length of pregnancy and pregnancy outcome dates reported in the questionnaire. In many cases, when the date of conception preceded father's first exposure, the conceptuses were assigned to a no exposure category (control) even though the father was in the dioxins group. Two new files were thereby created, one containing only "dioxins" conceptuses and one "non-dioxins" conceptuses; these files were used for subsequent analyses rather than those of the original exposed and non-exposed employees.

Variables

Dependent (outcome) variables were based on the three possible mutually exclusive pregnancy outcomes of live births, miscarriages, and stillbirths. For this study, induced abortions were omitted as outcomes, although they were considered in assigning gravidity scores to subsequent pregnancies. A miscarriage or spontaneous abortion was defined as a non-induced conceptus death with reported length of pregnancy of 20 weeks or less. A live birth was defined as the complete expulsion or extraction of a fetus which breathed or showed other evidence of life. A stillbirth was a conceptus which terminated as other than a miscarriage or a live birth.

A favorable pregnancy outcome was defined as a live birth where the infant survived its first birthday, and was not reported to display a congenital malformation as defined below. Miscarriages, stillbirths, infant deaths, and live births with congenital malformations were considered as unfavorable or adverse outcomes. Infant deaths were live births where the infant died before its first birthday.

Birth defects, which were not necessarily mutually exclusive of infant deaths, were coded only among live births, and were analyzed as either health defects, congenital malformations, or as indicator malformations. A health defect was defined as a live birth reported by the mother to have a health problem of any nature. A congenital malformation was a report by the mother of one or more defects which could be coded to the 740–759.9 range of ICD-8. An indicator malformation was a report by the mother of one or more defects of a set of seven of the following defects (preceded by the ICD-8 code): 741, Spina bifida; 742, Congenital hydrocephalus; 749.0, Cleft palate; 749.1, Cleft lip; 749.2, Cleft palate with cleft lip; 755.0, Polydactyly; 755.1, Syndactyly; and 759.3, Down's syndrome. Thus, indicator malformations were a subset of congenital malformations which, in turn, constituted a subset of health defects. Since mothers and not health professionals were providing the data, it was felt initially that the readily recognizable indicator malformations would provide the most valid outcome measure of the three above. Live births with health defects not codeable as congenital malformations were included as favorable pregnancy outcomes if the infant survived its first birthday.

Independent variables consisted of four exposure categories derived from the industrial hygienist's estimates: TCDD Only, at any level; Any Dioxins (TCDD and others) at any level; Moderate-to-High levels of TCDD only; and, Other Dioxins only (no TCDD). The first two were further broken down into two duration of exposure subcategories: 12 months or less, and more than 12 months. With the break point of 12 cumulative months exposure to dioxins, each subcategory included about one-half of the category-specific conceptuses.

If exposure in a job preceded the calculated date of a conception, the cumulative duration of each type of exposure in months prior to conception was calculated. Conceptuses were considered exposed to TCDD alone only if the father experienced no non-TCDD dioxins exposures before the conception date; those exposed only to non-TCDD dioxins were similarly identified. Conceptuses of dioxins workers were transferred to the control group if there was no paternal exposure to any dioxins prior to conception. Conceptuses of women reporting a marriage date to an exposed husband more than 150 days after the estimated date of conception were also assigned to the control group, since the questionnaire did not ask which conceptions were fathered by the current husband. Conceptions in previous marriages were also assigned to the control group.

For those analyses using the mother as the observational unit, women were allocated into one of four groups: 1) wives of men never exposed, 2) wives whose last conception occurred before their husband's first exposure to dioxins, 3) wives with some conceptions occurring before and some after their husband's first exposure, and 4) wives with all conceptions occurring after their husband's first exposure. The only covariable used in the analyses based on mothers was the total number of conceptions.

Covariables for analyses on conceptus as the observational unit consisted of nine potential confounding variables or effect modifiers (28, 29) which were abstracted from questionnaires. Each covariable, a recent literature reference describing its role, and a description are as follows:

Age (30). Mother's age in years at time of conception was computed and then categorized as <18, 18–30, >30 years.

Birth control method (31). Use of contraceptives was determined as of time of conception, and included four possible alternatives: none, pills (of any kind), intrauterine device, or any other method.

Complications during labor and delivery (32). A large proportion of women reported complications or illnesses after onset of labor, ranging from toxemia to premature rupture of membranes. Interviewers could record two problems with labor and delivery for each conceptus but, because of the diversity of responses, they were treated as a single all-or-nothing measure, i.e., any complication reported for a given conception was taken as a positive response. This variable was only considered in statistical analyses of stillbirths and live births.

Conditions during pregnancy (33). The questionnaire permitted a maximum of three maternal medical conditions to be reported as having occurred during each pregnancy. As with complications during labor and delivery, above, a wide variety of responses were elicited, ranging from infectious diseases during pregnancy to diabetes; many could have been causally related to pregnancy outcome. Responses were reduced to a single binary variable, positive (any condition) or negative (no condition reported for any of the questions).

Medications or treatment during pregnancy (34). There were two questionnaire items regarding treatments during pregnancy. As above, responses to these items were transformed to a binary variable. Thus, reported treatments such as x-ray and minor medications were given equal weight as a positive response.

Alcohol consumption (35). The questionnaire solicited quantitative information about alcohol use during each pregnancy. Responses were divided into two categories: consumption of six or fewer drinks, or more than six drinks per week.

Gravidity (36). Three levels of responses were coded: first pregnancy, second or third pregnancy, or fourth or higher pregnancy. Conceptuses of the same pregnancy (twins) were assigned the same value for this variable.

High risk job (37). When women were questioned as to their work activities during pregnancy, some named jobs which might have presented a risk to the pregnancy. Responses were reduced to a binary term (risk, no risk) with risk including the following occupations: operating room technician, x-ray technician, bacteriologist, chemical production worker, cosmetologist, and dental assistant.

Smoking during pregnancy (38). Interviewers asked the numbers of cigarettes smoked daily during each pregnancy but, for analyses, respondents were grouped as nonsmokers (did not smoke at all during a particular pregnancy) or smokers (smoked at any level during pregnancy).

Statistical methods

For analyses based on the mother as the observational unit, the four groups of mothers were first stratified by their number of conceptions (1,2, . . . 8). The computer program PARCAT (39) was used to obtain various Mantel-Haenszel statistics based on the number of women in each stratum reporting 1,2, . . . 8 pregnancy outcomes of interest (table 2).

The remaining statistical analyses attempted to determine whether there were differences in the distribution of values of outcome variables between the exposed conceptuses and nonexposed conceptuses, after adjusting by stratification for the influences of pertinent covariables. The analyses also attempted to examine, for the independent variables of exposure to TCDD Only or to Any Dioxins, whether there were trends of increasing adverse pregnancy outcomes with increasing durations of exposure.

For 2 × 2 crude tests of exposure-outcome association, as well as for examination of stratum(covariable)-specific associations, chi-square statistics were generated. Where chi-square was not appropriate due to table sizes, Fisher's exact test was employed (40). Tests for trend in 2 × 3 tables employed chi-square one degree-of-freedom statistics with linear weights (40). The corresponding tests on stratified sets of tables used Mantel-Haenszel chi-square statistics (41) and extended Mantel-Haenszel statistics (42). Programs to generate all of the above were written in SAS and SAS PROC MATRIX (43).

A FORTRAN program by Thomas (44) was used for calculation of odds ratios and related statistics to supplement chi-square tests.

For stratified analyses, Thomas's program computed asymptotic maximum likelihood odds ratios and confidence limits using a modification of the Extended Cornfield Method (45). An asymptotic test of the normal deviate, calculated by Mantel-Haenszel estimates of expected value and variance, was used as the one-tailed main effects test of departure of the odds ratio from unity. An asymptotic chi-square test for homogeneity (departure of the stratum-specific odds ratios from the overall stratified estimate of the odds ratio) was also performed. The latter two tests yielded *p* values only.

For stratum-specific calculations, where table sizes were <500, Thomas's program yielded a maximum likelihood estimate of the odds ratio, 95 per cent confidence limits, and an exact test of the stratum odds ratio against unity, giving a one-tailed *p* value. Where table sizes were large, as was the case for crude contingency tables, asymptotic tests and estimates were produced instead of exact estimates.

The effect of covariables on the association between exposure and pregnancy outcome was based on their independent action, their interaction with other independent or covariables, and/or their distribution at the combinations of levels of independent variables and covariables. It was not expected that a particular covariable would have the same effect (if any) on one contingency table of exposure versus outcome as on another table with different measures of exposure or outcome. Therefore, for each of the 48 exposure-outcome analyses, the set of nine potential covariables was evaluated using a forward-selection algorithm adapted to categorical data by Higgins and Koch (46). This algorithm selected a covariable set by assessing the relative strength of association of each candidate covariable with the outcome variable at each level of the covariables already accepted into the study. However, instead of using sets of 2 × 2 tables, as did Higgins and Koch, our procedure used extended ($r \times c$, $r, c > 2$) chi-square, and Cochran-Mantel-Haenszel chi-square measures to select covariables. We omitted the independent exposure variable from the candidate set of variables until the selection was complete instead of allowing it into the model first. The selection procedure stopped when no further associations of covariable-outcome were found to be significant at the $\alpha = 0.10$ level.

TABLE 2

Distribution of conception frequencies of wives of the Dow Chemical Company Michigan Division Site employees unexposed and potentially exposed to dioxins during production operations, Midland, Michigan, 1939–1975

No. of conceptions	No. of women with conceptions placed relative to husband's first exposure									
	Group 1		Group 2		Group 3		Group 4		Total groups 2–4	
	Husband never exposed		All conceptions pre-exposure		Some conceptions pre-exposure		All conceptions post-exposure			
	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)
1	22	(7)	4	(4)	0	(0)	13	(12)	17	(5)
2	60	(18)	23	(23)	22	(15)	22	(21)	67	(19)
3	82	(25)	32	(31)	33	(22)	23	(22)	88	(25)
4	63	(19)	17	(17)	24	(16)	19	(18)	60	(17)
5	56	(17)	13	(13)	21	(14)	13	(12)	47	(13)
6	20	(6)	6	(6)	13	(9)	6	(6)	25	(7)
7	14	(4)	4	(4)	16	(11)	5	(5)	25	(7)
8	6	(2)	2	(2)	10	(7)	1	(1)	13	(4)
9+	9	(3)	1	(1)	12	(8)	4	(4)	17	(5)
	(88 conceptions)		(11 conceptions)		(128 conceptions)		(45 conceptions)		(184 conceptions)	
Total	332*		102		151		106		359*	
	(1274 conceptions)		(370 conceptions)		(742 conceptions)		(391 conceptions)		(1503 conceptions)	

* Twenty-four women, 13 in Group 1 and 11 in Group 2, 3, or 4 reported no pregnancies at interview.

RESULTS

As noted previously, interviews were obtained from 370 wives (63 per cent) of the 586 potentially exposed employees eligible for interview, and 345 (62 per cent) of the 559 eligible control employees. Among eligible members of two previously studied cohorts, a "chloracne cohort" (25) and a "2,4,5-T cohort" (26), participation rates in the current study were comparable (67 per cent and 59 per cent, respectively).

The distribution of conception frequencies among wives of unexposed (group 1) and exposed (group 2, 3 or 4) employees is shown in table 2. A total of 1274 conceptions were reported by unexposed women, and 1503 by women in the exposed groups. Eleven unexposed and 13 exposed workers' wives claimed no pregnancies at interviews.

To examine the potential for recall bias, comparisons of frequencies of various adverse pregnancy outcomes between group 1 (nonexposed) and group 2 (all conceptions pre-exposure) women were made. No chi-square statistics so generated were found to approach significance.

As a test for exposure effects using the mother as the observational unit, adverse outcome frequencies of group 1 (nonexposed) and of group 2 (all conceptions pre-exposure) women were compared with those of group 4 (all conceptions post-exposure) women. Again, no comparisons detected any significant differences.

The bulk of the analyses were based on the conceptus as the observational unit. The homogeneity of outcomes of group 1 and group 2 women demonstrated above suggested that conceptions of nonexposed women, and group 2 women, and all conceptions of group 3 women occurring prior to the date of first exposure could be pooled as a control group of conceptions. Two thousand thirty-one conceptions, including 1785 live births, were thus identified as being nonexposed, or "non-dioxins" conceptions. Seven hundred thirty-seven conceptions, including 637 live births, were similarly counted among group 4 women (all conceptions post-exposure) and among post-exposure pregnancies of group 3 women. These were identified as "dioxins-exposed" conceptions for subsequent analyses. Nine induced abortions were deleted from the analyses.

Characteristics of the "dioxins" and "non-dioxins" conceptions and their frequencies are listed in tables 3–5. Table 3 shows frequencies of the coded diagnoses for all congenital malformations or health defects and for infant deaths. The frequency distribution of covariable values for conceptuses in the TCDD Only, in the Any Dioxins, and in the unexposed groups, are listed in table 4. Some differences were obvious; there were proportionately more conceptuses with mothers who were older than 30 years of age, or who were gravida 4+ in the exposed group, while there were proportionately more conceptuses with mothers who were taking medications or who had an illness during pregnancy in the control group. All multiple births were twins, with 35 sets comprising a total of 70 twins. Twins were proportionately equally distributed among dioxins conceptuses (10 sets in 737 or 1.36 per cent) and non-dioxins conceptuses (25 sets in 2031 or 1.23 per cent).

Table 5 shows the frequencies of various adverse pregnancy outcomes or dependent variables for each paternal exposure category, and the rates and ratios per 1000 live births calculated from these numbers. It should be emphasized that data in table 5 are crude and represent frequencies which were not adjusted for the influence of any covariables.

Numbers were very small in the independent variable categories of Moderate-to-High TCDD and of Other Dioxins alone, and in the dependent variable category of Indicator Malformations. These will therefore not be considered further as separate categories in the sections on Re-

TABLE 3

Frequencies and classification of incidents of infant death and health defects among live births to wives of Dow Chemical Michigan Division employees unexposed and potentially exposed to dioxins during production operations, Midland, Michigan, 1939–1975

Classification of death or illness	ICD-8 codes	Frequency
I. Congenital malformations or health defects*		
All congenital anomalies	740–750.9	130
Spina bifida	741	1
Congenital anomalies of heart	746	12
Cleft palate and cleft lip	749	10
All others	743–5; 748; 750–9	107
Other causes of perinatal morbidity and mortality	778–9	17
Anoxic and hypoxic conditions NEC	776	14
Birth injury and difficult labor	764; 768; 772	12
Benign neoplasms and neoplasms of unspecified nature	227; 232	11
Intestinal obstruction and hernia	550–1; 560	9
All others	112; 172–3; 254; 275; 343; 373; 389; 427; 429; 482; 511; 520; 564; 572; 607; 685; 692; 738; 771; 775; 781	46
II. Infant deaths		
Anoxic and hypoxic conditions NEC	776	10
Other causes of perinatal morbidity and mortality	777	10
Congenital anomalies of heart, and other anomalies	746; 742; 748; 751; 759	5
Conditions of placenta and cord	770; 771	5
Pneumonia	485–6	5
All others	246; 254; 320; 323; 508; 593; 772; 775; 795; 796	13

* A single conceptus may have contributed none, one or two codeable diagnoses, so numbers will not add up to total live births.

sults and Discussion, although they were analyzed as such when possible, and the Moderate-to-High-TCDD category was, of course, included in the TCDD-Only category. Table 6 is a summary of the crude and adjusted odds ratios with their 95 per cent confidence limits. Table 6 also lists p values for tests of homogeneity among stratum-specific odds ratios. As shown, no statistically significant differences in proportions of adverse pregnancy outcomes were detected using crude or adjusted odds ratios from 2 × 2 summary tables. Similarly, although not shown, results of the analyses for the other two exposure categories (Other Dioxins alone, and Moderate-to-High TCDD alone) were not statistically significant. All Mantel-Haenszel chi-square values, as well as crude chi-square statistics, were low, having p values greater than 0.10. Crude and adjusted trend analyses based on the length-of-exposure categories described previously were also nonsignificant.

TABLE 4

Characteristics of pregnancy environments of 2768 conceptions classified as unexposed or potentially exposed to dioxins through paternal work experiences in Dow Chemical Michigan Division production areas, Midland, Michigan from 1939–1975

Covariable	Exposure category of conceptus					
	Any dioxin		TCDD[†] only		Unexposed	
	No.	(%)	No.	(%)	No.	(%)
I. Mother's age (years) at conception						
Under 18	8	(1)	4	(1)	113	(6)
18–30	539	(73)	322	(77)	1675	(82)
Over 30	190	(26)	92	(22)	243	(12)
II. Birth control method used at time of conception						
None	658	(89)	378	(90)	1884	(93)
Pills	14	(2)	6	(1)	12	(1)
Intrauterine device	5	(<1)	1	(<1)	7	(1)
Other	60	(8)	33	(8)	128	(6)
III. Complications or illnesses during labor and delivery[*]						
None	456	(72)	271	(74)	1278	(72)
Any	181	(28)	97	(26)	507	(28)
IV. Health problems of mother during pregnancy						
None	482	(65)	269	(64)	1447	(72)
Any	255	(35)	149	(36)	584	(28)
V. Mother's medication or treatment during pregnancy						
None	473	(64)	257	(61)	1382	(68)
Any	264	(36)	161	(39)	649	(32)
VI. Mother's average weekly alcohol intake during pregnancy						
Six or fewer drinks	721	(98)	405	(97)	2020	(99)
More than six drinks	16	(2)	13	(3)	11	(<1)
VII. Gravidity						
1st pregnancy	96	(13)	62	(15)	603	(30)
2nd or 3rd pregnancy	297	(40)	186	(45)	890	(44)
4th or higher pregnancy	344	(47)	170	(41)	538	(26)
VIII. Did mother work in high risk activity during pregnancy						
No	726	(99)	416	(100)	2008	(99)
Yes	11	(<1)	2	(<1)	23	(1)
IX. Mother's smoking pattern during pregnancy						
Nonsmoker	528	(72)	320	(77)	1566	(77)
Smoker	209	(28)	98	(23)	465	(23)

[*] Applies only to live births and stillbirths (not to spontaneous abortions).

[†] TCDD, 2,3,7,8-tetrachlorodibenzo-p-dioxin.

Although none of the overall odds ratios, crude or adjusted, were statistically significant, there was noticeable lack of homogeneity among stratum-specific odds ratios for some of the exposure-outcome associations shown in table 6. This occurred among the outcome categories of Spontaneous Abortions, all Conceptus Deaths, and all Unfavorable Outcomes for the Any Dioxins exposure category, and among the same three for the TCDD-Only category. Consequently, all covariable-specific subtables for these six exposure-outcome combinations were examined for significant associations. Seven such associations were found, five with odds ratios greater than one, and two with odds ratios less than one. Recurrent

TABLE 5

Frequencies and rates or ratios (per 1000 live births) of pregnancy outcomes of 2768 conceptions classified as unexposed or exposed to dioxins through paternal work experiences in Dow Chemical Michigan Division production areas, Midland, Michigan, from 1939–1975

Pregnancy outcome	Exposed								Control	Total
	TCDD† alone				Other dioxins alone	Any dioxin				
	Moderate to high	Any level								
		<1 year	>1 year	Total		<1 year	>1 year	Total		
Conceptus deaths										
Miscarriage	0	18	25	43	0	36	49	85	213	298
(Ratio)	(00.0)	(108.4)	(123.8)	(116.8)	(00.0)	(112.5)	(154.6)	(133.4)	(119.3)	(123.0)
Stillbirth	0	3	4	7	0	8	7	15	33	48
(Ratio)	(00.0)	(18.1)	(19.8)	(19.0)	(00.0)	(25.0)	(22.1)	(23.5)	(18.5)	(19.8)
Total	0	21	29	50	0	44	56	100	246	346
(Ratio)	(00.0)	(126.5)	(143.6)	(135.9)	(00.0)	(137.5)	(176.7)	(157.0)	(137.8)	(142.9)
Live births										
Health defect	2	18	14	32	2	26	26	52	155	207
(Rate)	(181.8)	(108.4)	(69.3)	(87.0)	(100.0)	(81.3)	(82.0)	(81.6)	(86.8)	(85.5)
Congenital malformation	0	14	7	21	1	19	11	30	87	117
(Rate)	(00.0)	(84.3)	(34.7)	(57.1)	(50.0)	(59.4)	(34.7)	(47.1)	(48.7)	(48.3)
Indicator malformation	0	1	1	2	0	1	2	3	10	13
(Rate)	(00.0)	(06.0)	(05.0)	(05.4)	(00.0)	(03.1)	(06.3)	(04.7)	(05.6)	(05.4)
Infant death	0	4	2	6	1	7	2	9	39	48
(Rate)	(00.0)	(24.1)	(09.9)	(16.3)	(50.0)	(21.9)	(06.3)	(14.1)	(21.8)	(19.8)
Total unfavorable*	0	16	8	24	2	24	12	36	120	156
Total favorable	11	150	194	344	18	296	305	601	1665	2266
Total	11	166	202	368	20	320	317	637	1785	2422
All conceptions										
Total unfavorable	0	37	37	74	2	68	68	136	366	502
(Rate)	(00.0)	(197.9)	(160.2)	(177.0)	(100.0)	(186.8)	(182.3)	(184.5)	(180.2)	(101.4)
Total	11	187	231	418	20	364	373	737	2031	2768

* Unfavorable outcomes include only malformations with ICD-8 codes 740–759.9.

† TCDD, 2,3,7,8-tetrachlorodibenzo-p-dioxin.

TABLE 6

Crude and covariate-adjusted estimates of risk for adverse pregnancy outcomes among 2768 conceptions unexposed or potentially exposed to dioxins through paternal work experiences in Dow Chemical Michigan Division production areas, Midland, Michigan, from 1939–1975

Dependent variable	Crude Risk		Risk Adjusted by Stratification of Covariates		
	Odds ratio	(95% confidence limits)	Odds ratio	(95% confidence limits)	p (homogeneity of subtables)
I. Exposure to any dioxin					
All conceptus deaths	1.14	(0.88, 1.47)	1.03	(0.78, 1.37)	< 0.01
Stillbirths	1.27	(0.66, 2.45)	1.06	(0.54, 2.09)	0.20
Spontaneous abortions	1.12	(0.85, 1.47)	1.03	(0.77, 1.39)	0.02
Infant deaths	0.64	(0.29, 1.39)	0.63	(0.27, 1.39)	0.61
Health defects	0.93	(0.66, 1.31)	0.85	(0.60, 1.21)	0.57
Congenital malformations	0.96	(0.62, 1.50)	0.85	(0.53, 1.35)	0.62
All unfavorable outcomes[*]	1.03	(0.82, 1.29)	0.97	(0.76, 1.22)	0.05
II. Exposure to TCDD[†] only					
All conceptus deaths	0.99	(0.70, 1.40)	1.02	(0.71, 1.47)	0.09
Stillbirths	1.03	(0.41, 2.45)	0.97	(0.38, 2.36)	0.37
Spontaneous abortions	0.98	(0.68, 1.40)	0.96	(0.65, 1.42)	0.06
Infant deaths	0.74	(0.28, 1.85)	0.82	(0.30, 2.09)	0.42
Health defects	1.00	(0.66, 1.52)	0.93	(0.60, 1.43)	0.60
Congenital malformations	1.18	(0.70, 1.97)	1.08	(0.63, 1.83)	0.86
All unfavorable outcomes[*]	0.98	(0.74, 1.30)	0.98	(0.72, 1.32)	0.06

[*] Unfavorable outcomes include only malformations with ICD-8 codes 740–759.9.

[†] TCDD, 2,3,7,8-tetrachlorodibenzo-p-dioxin.

in the subtables with significantly elevated odds ratios was a group of nine TCDD-exposed conceptions which contributed three spontaneous abortions and only six live births to the analyses. Mothers of these conceptuses characteristically were 18–30 years of age, gravida 4+, were not using birth control methods at conception, reported no illnesses during pregnancy, did not work at high risk jobs, took medications during pregnancy, and had fewer than seven drinks per week. Except for slight differences in the pertinent covariable sets, TCDD-Only exposure is a subset of Any Dioxins exposure, and Spontaneous Abortions is a subset of Conceptus Deaths which, in turn, is a subset of Unfavorable Outcomes. Therefore, the nine conceptions account for much of the significant association in the other covariable-specific subtables. Detailed examination of subtables in the trend analyses gave similar conclusions.

Statistically significantly elevated or decreased odds ratios were not obtained for any other covariable-specific group. In fact, any changes in covariable category selection for the covariable-specific group described above (i.e., changing the age category, lowering gravidity, changing birth control usage to a different method or changing medications use from yes to no) not only eliminated statistical significance but in two cases significantly changed the direction of the association.

DISCUSSION

As detailed in the section on Results above, there were no statistically significant differences in crude or overall adjusted odds ratios for adverse pregnancy outcomes and any of the exposure categories, nor were there significant trends overall with increased duration of exposure on a crude or adjusted level.

The lack of an association of adverse pregnancy outcomes with differences in paternal exposure to dioxins may have at least five possible explanations: 1) differences did occur but were too small to be detected given the numbers involved and kinds of tests used; 2) differences did occur but could not be detected because of confounding by variables other than those considered; 3) differences did occur but were not detected because of inappropriate selection of exposed and unexposed populations; 4) differences did occur but were not detected because of weaknesses of the methods or errors in conduct of the study; or 5) paternal workplace exposures to dioxins were not associated with increased numbers of adverse pregnancies.

As regards the first possible explanation, ratios of adverse pregnancy outcomes have shown considerable unexplained fluctuations in almost every population which has been studied (47), and such fluctuations may have obscured differences here. From a purely pragmatic viewpoint, we could not have increased the power to detect differences by increasing the size of the exposed population since all employees with potential dioxins exposure were identified at the outset of this study. It might have been possible to increase power by increasing the number of controls (48), but the ratio of control conceptuses to exposed was already almost 3:1 (2031/737), and was even greater for exposure subsets. Despite these caveats, we did calculate the power (one minus beta error) possible at various levels of odds ratios for crude data in our study according to the program of Rothman and Boice (49). Depending upon which outcome was tested (and, hence, what the background or unexposed rates were), at $\alpha = 0.05$, the power to detect a crude odds ratio of 1.5 or greater varied from less than 50 per cent for Stillbirths, Indicator Malformations and Infant Deaths to 80 per cent or greater for all Conceptus Deaths, all Unfavorable Outcomes, and for Spontaneous Abortions. The power to detect odds ratios of two or greater was more than 90 per cent for these last three, whereas it was 70 per cent for Stillbirths, 98 per cent for Health Defects, 93 per cent for Congenital Malformations, 26 per cent for Indicator Malformations, and 61 per cent for Infant Deaths.

Unidentified covariables, if unequally distributed, may have obscured differences in pregnancy outcomes between exposed and control groups, even though we attempted to identify such variables and we chose statistical methods to handle confounding and effect modification. In addition, there is a practical limit to the number of variables which can be included in analyses.

Inappropriate selection of exposed and control populations can be a problem in any epidemiologic study. Lack of specific exposure data, and dilution of exposure groups with individuals who were not actually exposed could be considered weaknesses of any chemical industry epidemiologic studies. However, chemical exposures usually cannot be precisely documented. In the present study, exposed employees were selected on the basis of potential exposure to dioxins, and we attempted to quantify potential exposures as described previously. This quantification was relative because analytical methods sensitive enough to detect levels less than one part per million of dioxins were not available until refinements in gas chromatography were introduced in our analytical laboratories in the 1970's. However, since some employees in the high TCDD group had developed chloracne, there is relatively objective evidence that at least some had experienced fairly high exposures to dioxins. In addition, separation of the exposed group into two levels of duration of potential exposures permitted evaluation of dose-response.

It might be argued that controls selected from the same industry are inappropriate, but it is well known that employed persons differ in important health-related respects from the general population. Since the objective of this study was to identify effects of dioxins exposure rather than effects of other chemical exposures, it seemed reasonable that the control population be selected in exactly the same manner as the exposed.

There are weaknesses inherent in use of questionnaires to acquire epidemiologic data. Candidates for interview who were not available or eligible for interview or who refused to participate might, in fact, be the very persons most at risk. However, the refusal rates for both exposed and control wives were similar (198/568, 35 per cent and 194/540, 36 per cent) and there is no reason to suspect that reasons for noneligibility or refusal were different in the two groups. In addition, participation among the two previously studied cohorts mirrored the overall participation rates.

Bias of interviewers and respondents was possible, although an attempt was made to blind interviewers. To comply with the intent of informed consent, respondents knew the study concerned employees who had dioxins exposure and those who did not, but often the wife did not know whether her husband worked in a potential dioxins-exposed area or, if so, whether this applied to a particular pregnancy.

While statistical tests failed to reject the null hypothesis of no recall bias, it should be recognized that such a bias, if operating, would result in risk estimates erroneously elevated. However, there were no overall risk estimates that were statistically significantly elevated. We tried to avoid interpretation variation and related errors by having the same individual handle all data coding for computer input.

The analytical methods were selected as best suited for the multiple analyses needed for the many dependent and independent variables and covariables. Fitting covariable questionnaire data into categories may not always have been appropriate; for example, some illnesses and some medications could be considered more important than others. In addition, the variable selection procedure for assessing the relative strengths of association between covariables and outcome was not always appropriate because of heterogeneity of component strata. Small table sizes, particularly for subtables, often resulted in numbers insufficient for statistical analyses. Nevertheless, the variable selection process used seemed a reasonable compromise between an all-possible-combinations approach, where every level of every covariable is treated independently, and a complete modeling approach. That the method used was, in fact, capable of detecting differences was demonstrated by identification of a covariable-specific group with odds ratios statistically significantly different from one at the $\alpha = 0.05$ level as reported in the results.

We are uncertain as to why the covariable-specific groups in question should have yielded elevated odds ratios. One possibility was that subcategories within both the dependent and independent variables were not mutually exclusive. Spontaneous Abortions are a subset of Conceptus Deaths which are, in turn, a subset of Unfavorable Outcomes. In addition, the TCDD-Only exposure category is a subset of Any Dioxins exposure. In fact, a large component of the significant associations could be traced to nine conceptuses in the TCDD-Only exposed group with three spontaneous abortions and only six live births mentioned previously. By contrast, there were only one spontaneous abortion and 41 live births among the controls for this covariable-specific group. The relatively high number of abortions (for this study) in these exposed and the unusually low number in the controls accounted for some of the magnitude of the observed odds ratios.

Another possibility was that of the positive results occurring by chance because of the large number of analyses performed on the data. Theoretically, 73,728 2 × 2 tables were possible since there were totals of eight possible dependent variables, four possible independent or exposure variables and nine possible covariables. Six of these covariables had only two possible levels, but two (age and gravidity) had three and one (birth control method) had four. However, the covariable selection procedure reduced this possible number to 3505 and, of these, many tables either would have included no conceptuses at all or none in one of either the dependent or independent category levels. As a result, only 259 tables were actually tested, and odds ratios from only seven were found to be statistically significantly different from unity: five were significantly elevated and two significantly decreased. In the trend analyses, there were 36,864 theoretically possible tables, 2058 remained after covariable selection and 200 tables were actually prepared and tested; of these, six showed a statistically significant trend of increasing odds ratios with increased durations of exposure. As noted below, these positives were based on the same covariable-specific groups which were already positive in the 2 × 2 tables.

Statistically significant odds ratios were all for the dependent variables of Spontaneous Abortions, Conceptus Deaths, or Unfavorable Outcomes except in the case of the two decreased odds ratios which were for Spontaneous Abortions and Infant Deaths. In all cases, the covariable-specific groups of conceptuses were from women between the ages of 18 and 30 years, who did not use birth control methods, drank six or less alcoholic drinks per week and, except for one table, did not have a high risk job during pregnancy.

An alternative explanation to those preceding, of course, is that there was a real exposure effect which, for some reason, was limited to the covariable-specific group described. This is inconsistent with the overall nonpositive results of the study.

The fifth and last explanation offered for our results, that there were no differences in adverse pregnancy outcomes, is consistent with what is known of biological effects of the dioxins. While the experimental literature suggests that maternal exposures to some levels of TCDD may be associated with embryonic and teratogenic events in laboratory animals, the experimental literature also indicates that paternal exposures do not put conceptuses at excessive risk to unfavorable outcomes (7–9). The negative studies of humans exposed to relatively high levels of TCDD in Seveso, Italy, reinforce the laboratory data (20–24).

In conclusion, it is our interpretation that, under the conditions of this study, there were no biologically meaningful associations between adverse pregnancy outcomes and paternal dioxins exposures.

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EXHIBIT 6 (1)

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DIOXIN AND REPRODUCTIVE EVENTS

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Polychlorinated dibenzodioxins, sometimes referred to as PCDD's or simply dioxins, may be formed during the combustion of fossil fuels, the incineration of municipal wastes, or the production of chlorinated phenols.[1] Of all of the isomers of dioxins, 2,3,7,8-tetrachlorodibenzodioxin or TCDD, a low level contaminant of 2,4,5-T, trichlorophenol and its by-products, is considered the most toxic.[2]

A variety of biological effects have been indicated or hypothesized to be associated with exposures to TCDD. One set involves the potential influence of this chemical on reproduction. Animal experiments suggest adverse reproductive events may be associated with maternal exposures, but not with those of the father.[3,4,5] Reports of observational studies of humans are somewhat conflicting. The National Academy of Sciences, commissioned to study the effects of herbicides in South Vietnam, found no conclusive evidence of an association between exposure to herbicides and birth defects in humans.[6] Field and Kerr, in an ecological study in Australia, purported to have found a "linear correlation" between neural tube defects and increased use of the herbicide 2,4,5-trichlorophenoxy acetic acid (2,4,5-T), an agricultural chemical contaminated by low levels of TCDD.[7] On the other hand, Thomas reported that in Hungary, where 2,4,5-T usage had increased dramatically between 1970 and 1976, the frequency of stillbirths and congenital malformations had remained stable or decreased.[8] Smith recently published a "preliminary report of reproductive outcomes among pesticide applicators using 2,4,5-T in New Zealand".[9] No significant differences were found in the rates of congenital defects, stillbirths, and miscarriages between the chemical applicators and a control group.

There have also been dioxin-related claims of congenital malformations among offspring of United States and Vietnamese veterans of the Vietnam conflict who were exposed to aerial herbicides sprayings;[10,11] and of increased spontaneous abortions among women residing in or near areas of Oregon sprayed with 2,4,5-T.[12] None of these allegations have been substantiated epidemiologically and the Oregon spontaneous abortion data, when subjected to critical review, were found not to support the conclusion of an association with herbicide usage.[13]

Dow Chemical USA has conducted a series of epidemiological studies of employees potentially exposed to dioxin.[14,15] The following is a summary of a paper by Townsend et al, which has been submitted for publication.[16] It describes the results of an interviewer-administered questionnaire survey conducted among women whose husbands were employees of the Michigan Division of Dow Chemical U.S.A. The purpose of the survey was to compare the proportion of adverse outcomes between pregnancies associated with potential paternal exposures to 2,3,7,8-TCDD or other polychlorinated dioxins, and pregnancies with no known exposures to these chemicals.

MATERIALS AND METHODS

Selection of Study Subjects

Identification of wives whose husbands had been potentially exposed to dioxins, and of those whose husbands had not, was accomplished via company records. Using annual personnel census lists and individual work histories, employees who had been assigned to chlorophenol processes for at least one month between January 1939 and December 1975 were identified. By this criterion, there were 930 male employees with potential occupational dioxin exposures.

A comparable number of controls was selected from male employees who had no job assignments in the potential exposure areas, and who closely matched exposed employees by date of hire. By a variety of methods, addresses were obtained on all but 69 (3.7 percent) of the 1830 men. For the purposes of study efficiency, followup was limited to those who lived in Midland or adjacent counties. In the exposed group, 586 had wives potentially available for interview and 370 or 63% agreed to participate. Among the control group, 559 wives were potentially available and 345 or 62% were interviewed.

Estimation of Exposures

Manufacture of pentachlorophenol started at the Michigan Division of Dow Chemical, U.S.A. in 1939. Trichlorophenol production started in 1946. In late 1963, a change was made in the trichlorophenol process and shortly thereafter a number of employees contracted chloracne. Operations were modified to reduce exposures and, in 1966, trichlorophenol production was transferred to a new building.

Estimation of exposures was made by an industrial hygienist who was familiar with the processes. Based on his experience, information provided by production personnel and surface contamination data, each job was assigned an exposure potential on a scale of low to high for TCDD, for all other dioxins, or for mixed exposures.

Collection and Analysis of Data

A letter explaining the purpose of the study and requesting a personal interview was mailed to the residence of each living exposed or control population member residing in Midland or adjacent counties. Appointments were made with those women willing to be interviewed. If the employee was widowed or single, or if the response indicated the wife did not wish to be interviewed, no further action was taken.

Interviews were conducted in the home by one of three trained nurse-interviewers. Appointments were arranged by geographic clusters and not by exposure status. The interviewers did not know whether they were interviewing the wives of exposed or control empolyees. At the time of the interview, the intent of the study was re-explained, each woman was advised regarding confidentiality of the information and was asked to sign an informed consent. A five-page questionnaire was used and the interview normally took less than one half-hour.

Responses dealing with health defects, congential malformations and infant deaths were coded by the Eighth Revision of the International Classification of Diseases (ICD-8).[9] Each positive response regarding congenital malformations was coded if the mother stated the condition was diagnosed prior to one year after birth or if the mother was unclear as to the time of diagnosis. Conditions identified after the first birthday were reviewed by two physicians. If either physician, blinded as to the mother's group, determined the defect could have been diagnosed during the first year of life, the condition was so coded. Since these procedures were weighted toward identifying abnormalities, the resulting data could not be meaningfully compared with state or national statistics.

For the main purposes of this study, the individual conceptus or product of conception was the observational unit, taken as independent of other conceptuses of the same pregnancy or other pregnancies of the same or different womrn. Effect of exposure to dioxins was considered to be an irreparable event; that is, any exposure of a male employee any time prior to the estimated date of each conception attributed to him was investigated as an independent variable with potential effects on the pregnancy outcome. Conception dates were estimated from the length of pregnancy and pregnancy outcome dates reported in the questionnaire. When the date of conception preceded the father's first exposure, the conceptus was assigned to the no-exposure category even though the father was in the dioxins group. This prevented a dilutional effect on the risk estimates, while simultaneously making maximum use of the available data. Two new files were thereby created, one containing only "dioxins" conceptuses and the other "non-dioxins" conceptuses.

Variables

Dependent variables included live births and the adverse outcomes of miscarriages, stillbirths, infant deaths, and live births with congenital malformations. Birth defects were analyzed as either health defects, congenital malformations, or as indicator malformations. A health defect was defined as a live birth reported by the mother to have a health problem of any nature. A congenital malformation was a report by the mother of one or more defects in the 740-759.9 range of ICD-8.[17] And an indicator malformation, one that we felt would be readily observed by the mother, was any one of the following (preceded by its ICD-8 code):

741.0	Spina Bifida
742.0	Congenital Hydrocephalus
749.0	Cleft Palate
749.1	Cleft Lip
749.2	Cleft Palate with Cleft Lip
755.0	Ploydactyly
755.1	Syndactyly, and
759.3	Down's Syndrome

Thus, indicator malformations were a subset of congenital malformations which, in turn, constitute a subset of health defects.

Independent variables consisted of four exposure categories:

TCDD Only, at any level

Any Dioxins (TCDD and others), at any level

Moderate to High TCDD Only, and

Other Dioxins Only (no TCDD).

The first two were also broken down into two duration-of-exposure subcategories: equal to or less than one year, and greater than one year total exposure.

Covariables were nine potential confounding factors or other reasons for adverse reproductive outcomes referenced in the literature: age, birth control method, complications during labor and delivery, conditions during pregnancy, medications or treatment during pregnancy, alcohol consumption, gravidity, high risk job, and smoking during pregnancy (Table 1). You will note from the Table, many were broken down into subcategories. Complications during labor and delivery were only considered a potential confounder for the analysis of stillbirths. High risk jobs were those held by the mother during pregnancy, such as operating room technician, x-ray technician, bacteriologist, cosmetologist, and dental assistant. Smoking was confined to that pregnancy, and not life-time experience.

Statistical Analysis

Statistical analyses attempted to determine whether there were differences in the distribution of outcomes between the "exposed" and "non-exposed" conceptuses. This was done on crude or unadjusted outcomes, and after adjusting by stratification for the influences of pertinent covariables. Trend analyses were also examined for the exposures to TCDD Alone or to Dioxins Of Any Type, that is, whether there were trends of increasing adverse pregnancy outcomes with increasing durations of exposure.

RESULTS

Interviews were obtained from 370 wives of potentially exposed and 345 wives of control employees (Table 2). Eleven in the first group and 13 in the second reported no pregnancies, 3.0 and 3.8 percent, respectively. A total of 1503 conceptions occurred among wives of the exposed and 1274 among those of the unexposed, or 4.06 and 3.69 conceptions per woman, exposed and unexposed.

As mentioned earlier, most of the analyses used the conceptus as the observational unit. Therefore, those conceptuses conceived by an "exposed" employee prior to his exposure to dioxin were considered to be "non-exposed" conceptuses and placed in the control pool for the purposes of the analyses. As illustrated diagrammatically in Figure 1, the consequence of this strategy was an increase in the number of "non-exposed" and a corresponding decrease in the number of "exposed" conceptuses. The 370 wives of employees exposed some time between 1939 and 1975, had a total of 1503 conceptions, but only 737 occurred after their husbands' first exposure to dioxin. These 737 constitute the "exposed" conceptuses. Thus, 1503 minus 737 or 766 conceptions occurred before the father was employed in a dioxins area.

We had two options with regard to the data on the 766. We could throw the data away, or add the experience of those 766 "pre-exposure" conceptuses to the 1274 conceptuses that occurred among wives of never exposed employees. We chose the latter. That gave us 766 plus 1274 or a grand total of 2040 conceptuses in the "unexposed" category. There were 9 induced abortions among this latter group, which reduced the number to 2031. The rest of the discussion

Table 1. Covariables

Age
<18, 18-30, >30 Years
Birth Control
None, Pills, IUD, Other
Complications During Labor and Delivery
Conditions During Pregnancy
Medications
Alcohol
≤6 or >6 Drinks Per Month
Gravidity
1, 2 or 3, > 3
High Risk Job
Smoking

Table 2. Summary of Pregnancies

	Exposed	Unexposed
Interviews	370	345
No Pregnancies		
Number	11	13
Percent	3.0	3.8
Conceptions		
Number	1503	1274
Mean	4.06	3.69

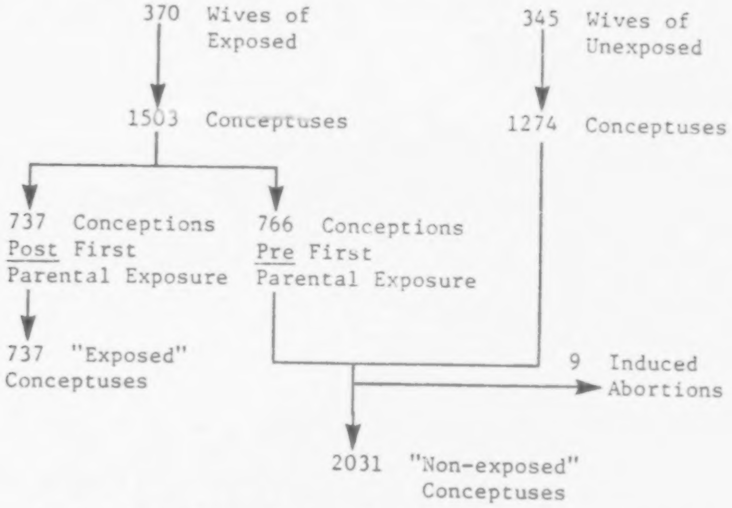
370 Wives of Exposed
345 Wives of Unexposed
1503 Conceptuses
1274 Conceptuses
737 Conceptions Post First Parental Exposure
766 Conceptions Pre First Parental Exposure
737 "Exposed" Conceptuses
9 Induced Abortions
2031 "Non-exposed" Conceptuses

Figure 1. "Exposed" and "Non-exposed" Conceptuses

concerns the comparison of the 737 "exposed" conceptuses to the 2031 "unexposed".

Tables 3 and 4 provide crude and adjusted measures on Any Dioxin and TCDD Only. None of the odds ratios for Any Dioxin (Table 3) were significantly elevated, either crude or after adjustment for pertinant confounders. There was a notable lack of homogeneity among some of the subtables: all conceptus deaths, spontaneous abortions, and unfavorable outcomes.

For TCDD Only (Table 4), none of the odds ratios were significantly elevated. Notice that some of the odds ratios, All Conceptus Deaths and Infant Deaths, increased slightly after adjustment. Notice also that the subtables, for the same three dependent variables - All Conceptus Deaths, Spontaneous Abortions, and Unfavorable Outcomes, are marginally non-homogeneous.

The covariable-specific subtables for these exposure-outcome combinations that showed evidence of non-homogeneity were examined for significant associations, some 123 in number. Seven such associations were found; five with odds ratios greater than one, and two with odds ratios less than one. Recurrent, in the subtables with elevated odds ratios, was a group of 9 TCDD-exposed conceptuses who contributed 3 spontaneous abortions and only 6 live births to the analyses. Mothers of these conceptuses characteristically were 18-30 years of age, gravida 4+, were not using birth control methods

Table 3. Crude and Adjusted Odds Ratios, P Values and Homogeneity of Subtables, All Outcomes, Any Dioxin

	Crude		Adjusted		
Outcome	Or	P	Or	P	Homogenity (P)
All Conceptus Deaths	1.14	.31	1.03	.44	<.01
Stillbirths	1.27	.26	1.06	.49	.20
Spontaneous Abortions	1.12	.23	1.03	.44	.02
Infant Deaths	0.64	.15	0.63	.15	.61
Health Defects	0.93	.37	0.85	.20	.57
Congenital Malformations	0.96	.48	0.85	.62	.62
All Unfavorable Outcomes	1.03	.42	0.97	.41	.05

Table 4. Crude and Adjusted Odds Ratios, P Values, and Homogenity of Subtables, All Outcomes, TCDD Only

	Crude		Adjusted		
Outcome	Or	P	Or	P	Homogenity (P)
All Conceptus Deaths	0.99	.93	1.02	.49	.09
Stillbirths	1.03	.54	0.97	.56	.37
Spontaneous Abortions	0.98	.49	0.96	.45	.06
Infant Deaths	0.74	.32	0.82	.41	.42
Health Defects	1.00	.54	0.93	.40	.60
Congenital Malformations	1.18	.30	1.08	.43	.86
All Unfavorable Outcomes	0.98	.47	0.98	.47	.06

at conception, reported no illnesses during pregnancy, did not work at high risk jobs, took medications during pregnancy, and had fewer than seven drinks per week. Since TCDD Only was a subset of Any Dioxin, and Spontaneous Abortions was a subset of All Conceptus Deaths, which, in turn, was a subset of All Unfavorable Outcomes, it is probably not surprising that this one covariable-specific group produced such a ripple effect. I should note that a shift of even a single covariable eliminated statistical significance and, in some cases, changed the direction of the association.

Not shown are the results for the categories moderate-to-high TCDD and other dioxins above. Their numbers were quite small, but none of the results were statistically significant; each, of course, was a subset of at least one of the categories shown. Crude and adjusted trend analyses based on length-of-exposure categories were also non-significant.

DISCUSSION

In summary, there were no statistically significant differences in crude or adjusted risk estimates for any of the pregnancy outcomes studied. Nor were there significant trands overall with increased duration of exposure.

The observed lack of association of adverse pregnancy outcomes with differences in paternal exposure to dioxins may have a variety of explanations. There may have been problems related to selection, misclassification, confounding or power that prevented us from picking up true differences in the two groups.[18,19] These are, of course, problems with any epidemiological study and are discussed in the referenced report.[16]

In addition, there may have been a problem with recall bias. That is, those among the wives of the exposed, having been informed of the intent of the study prior to the interview, may have ruminated about adverse outcomes and reported more, relatively, than did the controls. This would have produced an artificial elevation in some or all of the risk estimates.

It is also possible that the results reflect the true state of nature; that is, there is no risk to human reproduction caused by paternal exposures to dioxins. This explanation is consistent with most of the animal and human data we have to date.

In conclusion, it is our interpretation that, under the conditions of this study, there were no biologically meaningful associations between adverse pregnancy outcomes and paternal dioxin exposures.

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Trace Chemistries of Fire: A Source of Chlorinated Dioxins

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Summary. New, highly specific and sensitive analytical methodology has been applied to the determination of chlorinated dibenzo-*p*-dioxins in particulate matter. The results show that the dioxins are present in particles from many types of combustion sources and in dust and soil in the vicinity of combustion sources. The data indicate that chlorinated dioxins may occur in particulate matter from the combustion of most types of organic material, and suggest the hypothesis that chlorinated dioxins result from trace chemical reactions occurring in fire.

Polychlorinated dibenzo-*p*-dioxins have been found in fly ash from municipal incinerators by Olie *et al*. (*1*) in the Netherlands, by Buser *et al*. (*2*) in Switzerland, and by Eiceman *et al*. (*3*) in Canada, Japan, and the Netherlands. Buser also reported finding them in fly ash from an industrial heating facility. In all these studies the findings were qualitative and the presence of the dioxins was considered to be most probably caused by condensation of chlorophenols. Olie, however, suggested that a thermal synthesis from inorganic chloride and organic material was possible, and this route was supported by the presence of relatively large amounts of chlorinated benzenes on the particulate matter. Eiceman suggested that these compounds are formed during incineration processes.

This article presents quantitative data on particulate matter from a wide variety of combustion processes. These data cannot be satisfactorily explained in entirety by attributing the presence of polychlorinated dibenzo-*p*-dioxins to condensation of preexisting polychlorinated phenols.

The findings reported here are not offered as comprehensive or exhaustive results. Limiting factors include the small number of scientists specifically trained in the required methodology and the highly sophisticated instruments needed to conduct the work. In addition, the subject involves a large number of variables over which the investigators had no control.

Samples were not always taken by statistical design, and results are not intended to represent anything other than the sample analyzed. The analytical methodology developed so rapidly during this investigation that later results cannot always be directly compared to earlier ones. The analytical methodology including sampling has been reviewed by a group of scientists (*4*), however, and found to represent the state of the art. The results as a whole verify scientific observations that are now emerging worldwide.

Discovery

Chlorinated dioxins appear to be ubiquitous. Their ubiquity is due to the existence of natural phenomena, trace chemistries of fire which consist of numerous chemical reactions occurring during combustion at concentrations as low as 10^{-10} percent. We include two major pathways in these trace chemistries of fire, involving (i) chemicals present in higher concentration and reacting at very low yields (10^{-10} percent) and (ii) chemicals present in trace concentration and reacting at higher yields (10^{-4} percent).

A variety of research organizations have addressed themselves to the investigation of combustion processes. However, virtually all of their work has been concerned with the kinetics and thermodynamics of the fuels, oxidants, major intermediates, or major products. Mention should be made of several recent reviews of these investigations (*5*), although none of them discuss either pathway described above.

In an attempt to determine the source of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) that we detected in some fish from the Tittabawassee River (*6*), we examined the local as well as more distant environments and found that a large number of sources emit chlorinated dioxins into the environment. Samples were gathered from incinerator stacks as well as from chemical tar burners and a fossil-fueled power plant, vehicle mufflers, fireplaces, chimneys, cigarette smoke, and portions of charcoal-broiled steaks.

Chlorinated dioxins were found in each sample. However, those on particulate matter taken from the air emissions of a wide variety of commercial and domestic combustion processes are especially significant. Combustion processes must be more than 99.9 percent efficient to ensure reduction of the concentration

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Table 1. Chlorine content of fuels [summarized from (7)].

Fuel	Chlorine (ppm)
Coal	1300 (mean)
Refuse	2500 (average)
Paper	300 to 1600
Leaded gasoline	300
Unleaded gasoline	1 to 6
Fuel oil	N.A.*

*N.A., not available. Data were not available for the chlorine content in fuel oil. However, measurements indicated that 500 pounds of hydrogen chloride would be produced per day per 100,000 persons whose homes were heated by oil-fired furnaces.

of the dioxin from 1 part per million (ppm) to 1 part per billion (ppb). Common combustion processes are not adequate (*5*).

Building Blocks for Chlorinated Dioxins

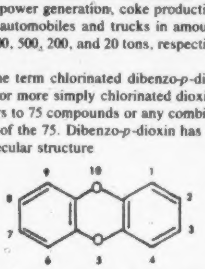
Refuse and fossil fuels are extremely complex mixtures of many chemicals and compounds, some of which are present at low concentrations. The chlorine content of various materials used as fuels for combustion has been examined by a committee sponsored by the National Academy of Sciences (*7*). Table 1 summarizes the result of that survey. The National Academy of Sciences estimated that "311 ppm of chlorine, mostly hydrogen chloride, is in flue gas from burning normal base refuse." Some of this chlorine is found on the fly ash accompanying the flue gas.

Fly ash from a municipal incinerator in Amsterdam was examined for chlorinated aliphatic and aromatic hydrocarbons by Lahaniatis *et al*. (*8*). More than 77 gas chromatography (GC) peaks, representing concentrations of 5 to 250 ppb, were obtained with an electron capture (EC) detector. Mass spectrometry (MS) provided identification of 27 of these peaks and empirical formulas for 22 more. Lasiewicz and Logensda (9) reported the following percentages of solid and gaseous products in emissions from oil-fired heating and power plants: sulfur dioxide, 1 to 6; sulfuric acid, 1 to 6; carbon monoxide, 0.1 to 0.2; nitrogen oxides, 0.5 to 1; dust, 0.2 to 1; vanadium compounds, 0.005 to 0.01; nickel oxide, 0.001 to 0.003; and soot, 0.1 to 0.5. Particles emitted from coal-fired boilers were shown by Kobayashi and Ibezawa (*10*) to contain 3,880 to 38,700 ppm vanadium, 1,810 to 98,500 ppm nickel, 1,440 to 19,200 ppm iron, and about 270 ppm manganese.

The data show that the myriad of initial pyrolysis products formed during combustion are jumbled at low concentrations in a sea of chemical reactions including pyrolysis, oxidation, reduction, and acidolysis which result from interaction of ions, electrons, free radicals, and free atoms. Up to now, the behavior of this chemical potpourri has been studied only in terms of the major products of combustion—water and carbon dioxide—and those generally described as minor—carbon monoxide, hydrogen chloride (*7*), sulfur oxides (*11*), and nitrogen oxides (*12*). This situation is further complicated by the use of water to quench or scrub the combustion gases. Donaldson (*13*) points out that water treated for domestic consumption contains about 1000 ppb organic chemicals. Commonly used waters often contain higher amounts of organic chemicals. When the chemicals in scrubber waters come in contact with the gaseous reacting chemicals, many more trace chemicals may form.

One trace-level combustion product, benzo[*a*]pyrene (*14*), has been studied in some detail. Like chlorinated dioxins, it is found on particulate matter. It is formed in higher concentrations during inefficient burning, has a high melting point, and readily photodegrades in solution. It is highly stable on particulates and has a very low solubility in water. The best estimates (*14*) showed that in 1971 benzo[*a*]pyrene was produced in the United States by refuse burning, heat and power generation, coke production, and automobiles and trucks in amounts of 600, 500, 200, and 20 tons, respectively.

The term chlorinated dibenzo-*p*-dioxins, or more simply chlorinated dioxins, refers to 75 compounds or any combination of the 75. Dibenzo-*p*-dioxin has the molecular structure



It is said to be chlorinated if one or more of the hydrogen atoms at the 1, 2, 3, 4, 6, 7, 8, and 9 positions is replaced by a chlorine atom. The 75 different chlorinated dioxins, each of which has its own special properties, are listed in Table 2. In only a few cases have these compounds been synthesized and their chemical and physical properties studied. Only TCDD has been examined comprehensively for its toxicological effects (*14*).

Table 2. Chlorinated dioxins.

Chlorine substitution	Acronym	Number of positional isomers
Mono-	MCDD	2
Di-	DCDD	10
Tri-	T_3CDD	14
Tetro-	TCDD	22
Penta-	PCDD	14
Hexa-	HCDD	10
Hepta-	H_7CDD	2
Octa-	OCDD	1

Analytical methods for the determination of TCDD or other chlorinated dibenzo-*p*-dioxins have been evolving. We used primarily GC-MS for these determinations (*6*). By means of several liquid chromatographic (LC) cleanup procedures, we developed specific methods for the determination of each of the tetra-, hexa-, hepta-, and octa- compounds in environmental samples. Details of these methods are being published in a series of three comprehensive papers (*15*). Since some of the procedures were developed during the course of this work, we report results here under the general heading TCDD, which includes 2,3,7,8-TCDD and other isomers as outlined below:

1) Analytical method ML-AM-73-97 (LC plus GC-MS) discriminates 2,3,7,8-TCDD plus 16 other isomers (*16*).

2) Analytical method ML-AM-78-63 [high-pressure liquid chromatography (HPLC) plus GC-MS] discriminates 2,3,7,8-TCDD plus 11 other isomers (*17*).

3) Analysis by HPLC plus capillary GC-MS discriminates 2,3,7,8-TCDD plus two other isomers.

The data from the various investigations of environmental samples are summarized in Table 3. The samples are described in the following sections.

Soil and Dust

All soil samples listed in Table 3 were collected at the surface from open, undisturbed areas, 10 by 10 centimeters square and 1 centimeter deep; an effort was made to exclude grass and other debris. They were placed in clean bottles and sealed until they were analyzed. The first 13 samples collected in the Midland area were analyzed qualitatively. Octa- and heptachlorodibenzo-*p*-dioxins were detected in all the samples, hexachlorodibenzo-*p*-dioxins were detected in nine, and tetrachlorodibenzo-*p*-dioxins were found in only four. A second set of soil samples was taken from areas previously sampled. Five of these, including four corresponding to the samples that previously showed TCDD, were analyzed by analytical method ML-AM-78-63, which permitted separation of 2,3,7,8-TCDD from all but about 11 of its 21 isomers.

Interference was sometimes noted in the analysis of reagent blanks. To determine whether this was caused by contamination, dust samples were collected from the tops of bookcases, solvent storage cabinets, and hoods, and at the air intake of the Dow Chemical laboratory. Analytical method ML-AM-78-63 was used. Dust samples to be used as controls were also collected from Midland and Detroit and analyzed by method ML-AM-73-97 The concentration reported for TCDD includes 16 other isomers. The results of this random sampling did not satisfy the need for control samples. Samples of soil and dust were therefore collected from Chicago, Illinois, and from East Lansing and Gaylord, Michigan. A few of the TCDD results for Lansing and Chicago were confirmed by GC combined with high-resolution MS.

Other sources of environmental particulate material include "urban particulate matter," collected in St. Louis, Missouri, and distributed by the National Bureau of Standards as SRM 1648, and Milorganite, a sludge fertilizer from Milwaukee, Wisconsin. The results of these analyses are also shown in Table 3.

Incineration

The European findings of chlorinated dioxins in fly ash together with the results of our analyses of dust and soil led us to examine particulate matter from incinerators and a powerhouse.

Dow operates two major waste incineration systems within the Midland complex. The first is a stationary tar burner operating at 72 million Btu's per hour, which was constructed and started in 1970. This unit represents one of the most advanced designs in liquid tar incineration and is one of the largest in the world. It is equipped to burn supplemental natural gas automatically, should the burning quality of the tars be insufficient to maintain the desired combustion temperature. The other Dow system is a rotary kiln incinerator capable of incinerating solids and liquids and operating at 70 million Btu's per hour. Supplemental fuel is also burned in this unit in the rotary kiln and the secondary combustion chamber to maintain the desired combustion temperatures. Samples of particulate matter were taken from the stacks of both units, using a procedure based on Environmental Protection Agency (EPA) methods (*18*). The data

Table 3. Chlorinated dioxins in the environment.

Sample	Number of samples	Apparent dioxin content, ng/g (ppb)*					
		TCDD			HCDD	H_7CDD	OCDD
		Other isomers	2,3,7,8-	Total			
Soil							
Rural (Gaylord, Michigan)	5			N.D.†	N.D.	N.D.-0.05	N.D.-0.2
Urban (Lansing and East Lansing, Michigan)	5			N.D.	0.03-1.2	0.03-2	0.05-2
Major metropolitan (Chicago, Illinois)	8			0.005-0.03	0.03-0.3	0.1-3	0.4-22
Dow Chemical (Midland, Michigan)	5	0.8-18	0.3-100	1-120	7-280	70-3,200	490-20,000
Dust							
Dow Chemical laboratory	6	0.5-2	0.7-3	1-4	9-35	140-1,200	650-7,500
Midland, Michigan	2			0.03-0.04 (0.02)	0.2-0.4	2-4	20-30
Metropolitan (Detroit, Michigan)	4			N.D.-0.03	N.D.-0.3	0.3-4	0.1-4
Metropolitan (St. Louis, Missouri)	1	0.16	0.12	0.3	2	34	210
Metropolitan (Chicago, Illinois)	2			0.04 (0.04)	N.D.-0.3	0.6-3	3-8
Wastewater treatment sludge							
Commercial sludge fertilizer (Milwaukee, Wisconsin)	1	0.29	0.02	0.31	2	30	180
Incinerators, powerhouse							
Dow powerhouse	1	38 (20)	N.D. (10)	38 (20)	2	4	24
Dow rotary incinerator stack (present normal operation with supplemental fuel)‡	5			N.D. (2)	1-5	4-100	9-950
Dow stationary tar burner stack (normal operation with supplemental fuel)	5	N.D.	N.D.	N.D.	1-20	27-160	190-440
U.S. municipal incinerator (electrostatic precipitator) (Nashville, Tennessee)	1	7.3	0.4	7.7	14	28	30
European municipal incinerators				2-20	30-200	60-130	40-120
Mufflers							
Diesel truck muffler	2	0.02	0.003	0.023	0.020	0.100	0.26
Auto muffler	4	N.D.-0.004	N.D.-0.004	N.D.-0.008	N.D.	0.003-0.01	0.02-0.07
Other sources							
Home fireplace soot	2	N.D.-0.3	N.D.-0.1	N.D.-0.4	0.2-3	0.7-16	0.9-25
Home electrostatic precipitator	1	0.4 (0.4)	0.6	1.0	34	430	1,300
Cigarette smoke	2	N.D.	N.D.	N.D.	0.004-0.008	0.009	0.02-0.05
Charcoal-broiled steak	4	N.D.	N.D.	N.D.	N.D.	N.D.	0.03 (0.03)

*Where multiple samples were analyzed from similar sources, the range of observed values is shown. †N.D. indicates that the signal observed was less than 2.5 times noise. Limits of detection generally observed were TCDD, 0.001 to 0.01 ppb; HCDD, 0.01 to 0.05 ppb; H_7CDD, 0.005 to 0.03 ppb; and OCDD, 0.01 to 0.05 ppb. Limits of detection not within these ranges are shown parenthetically after the value reported for signals between 2.5 and 10 times noise. ‡Data without supplemental fuel not included here because this practice has been eliminated.

for the rotary kiln incinerator are given in Table 4. There is a dramatic difference in chlorinated dioxin concentration between runs with supplemental fuel and without supplemental fuel. The data for the stationary tar burner are summarized in Table 3.

An examination of particulate material collected by the electrostatic precipitator on a municipal refuse incinerator in Nashville, Tennessee, also confirmed the presence of chlorinated dioxins. Table 3 presents the results of this analysis. The performance of this and other currently licensed municipal incinerators has been described in a recent article on refuse fuel recovery (*19*).

Table 4. Chlorinated dioxin content of particulate matter from the rotary kiln incinerator.

Sample	Fuel*		Apparent dioxins, ng/g (ppb)				
	Kiln	Secondary	TCDD		HCDD	H_7CDD	OCDD
			Other isomers	2,3,7,8-			
			Without supplemental fuel				
R_1F_1	T, SW, G	T	1,800	2,800†	13,000	110,000	180,000
R_1F_2	T, SW, G		5,000	8,200†	65,000	510,000	810,000
R_2F_1	T, SW, G		3,300	110	1,300	2,000	3,000
R_3F_1	T, SW, G		12,000	N.D. (260)‡	5,600	37,000	59,000
			With supplemental fuel				
R_3	T, SW, G	O, G	N.D. (8.0)	N.D. (2.0)	1.4	13.0	30.0
R_4	T, SW, G		N.D. (7.0)	N.D. (5.0)	N.D. (1.0)	4.0	9.0
R_5	T, SW, G		N.D. (2.0)	N.D. (2.0)	N.D. (0.5)	6.0	15.0
R_6	T, SW, G	T, G	N.D. (2.0)	N.D. (4.0)	5.0	27.0	170.0
R_7	T, SW, G		N.D. (2.0)	N.D. (2.0)	4.0	110.0	950.0

*T, tars; SW, solid waste; G, gas; O, oil. †The high results reported for the 2,3,7,8- isomer are probably due to analysis by the nonspecific GC-MS packed-column method. Later results were obtained with a capillary column specific for 2,3,7,8-TCDD. The TCDD results from run 1 (R_1) are not comparable to those from runs 2 and 3. ‡Numbers in parentheses are limits of detection, as explained in a Table 3 footnote.

Table 5. Other identified chlorinated compounds.*

Sample source	Chlorinated dibenzofurans			Decachlorobiphenyl	Polychlorinated terphenyls
	Hexa-	Hepta-	Octa-		
Dow research building	++	++	++		++
Midland city		+	+		+
Fireplace soot		+	+		+
All soil samples		+	+		+
Electrostatic precipitator		+	+		+
Metropolitan area dust (Detroit)					+
Urban area soil (Lansing and East Lansing)		+	+		+
Metropolitan area dust					
Chicago		++	++		++†
St. Louis		+	+		+
Metropolitan area soil (Chicago)		++	++	++	+†

*(+) Positive according to retention time on a liquid chromatogram, GC-MS not used; (++) positive by both LC and GC-MS. †Very large amount relative to other samples.

Table 6. Chlorinated dioxins in rotary kiln incinerator scrubber water.

Sample	Apparent dioxins, ng/g (ppb)				
	TCDD		HCDD	H_7CDD	OCDD
	Other isomers	2,3,7,8-			
Particulates filtered from scrubber water					
Without supplemental fuel	300	2,200*	3,400	26,000	42,000
With supplemental fuel	14	32*	200	970	1,200
Filtered scrubber water without supplemental fuel	0.0018 (0.01)	0.001* (0.0006)	0.005	0.024	0.026

*The analytical method did not separate 2,3,7,8-TCDD from 11 other isomers.

Data on samples taken from the stack of a Dow Midland powerhouse operating under normal conditions with fuel oil and coal are presented in Table 3. Approximate data for the European municipal incinerators are also shown for comparison.

Combustion of Dioxins

Early in 1965 Dow analytical scientists showed that TCDD decomposes 99.95 percent at 800°C in a stream of air passing through an unpacked quartz tube containing the TCDD (*20*). Consequently, it was accepted that TCDD would be destroyed in a system such as a tar burner. A further study in 1970 (*21*) confirmed these results and also showed that the 2,3,7,8-tetra- isomer is stable below 800°C.

Another Dow study in 1970 (*19*) established that the combustion products of TCDD in a 150 percent excess of air are water, carbon dioxide, hydrogen chloride, and chlorine. The adiabatic flame temperature was calculated as 1025°C. At this temperature the HCl/Cl_2 mole ratio is 3.05/0.48. This study, coupled with the earlier studies, led us to conclude that, below 800°C, the destruction of TCDD is relatively incomplete.

In preparation for the incineration at sea of the mixture known as Agent Orange (*22*), the U.S. Air Force contracted with the Marquardt Company, Van Nuys, California, to conduct tests on the combustion of Agent Orange with firewall temperatures of 1150°, 1400°, and 1600°C and a minimum of 30 percent excess air. TCDD, a trace impurity in one of the components of Agent Orange, was not found in the particulate matter in either the stack or the scrubber water at limits of detection of 300 and 2 ppb, respectively. In these tests, the walls of the combustion chamber were preheated to the desired temperature (1400°C) and the Agent Orange was added without auxiliary fuel. The temperature of the flame was not measured.

The Air Force disposed of Agent Orange in the summer of 1977 by high-temperature incineration at sea on a Dutch-owned ship M/T *Vulcanus*. Although the walls of the combustion chamber were maintained at 1273°C on the average and the high flame temperature was measured optically as 1500°C, the EPA, which monitored this program, reported a combustion efficiency for TCDD of only about 99.9 percent (*23*).

Particulate Matter from Mufflers

Mufflers from gasoline-powered automobiles were collected at muffler shops in Pontiac and Detroit, Michigan (more than 100 miles from Midland), as they were removed from cars. The car owners voluntarily gave the mufflers and information about mileage and gasoline type used. The make, model, and mileage of each car were noted. The mufflers were transported to the Dow Analytical Laboratories sealed in plastic bags. Mufflers from diesel-powered trucks were collected at Auburn and Saginaw, Michigan. They were sealed and transported as above.

At the Dow Analytical Laboratories, the inside chambers of the mufflers were scraped and residue was collected from these chambers and analyzed for chlorinated dioxins by both GC with electron capture detection and GC-MS after liquid chromatographic separation. Results are summarized in Table 3. The discovery that there are chlorinated dibenzo-*p*-dioxins in particulate emissions from internal combustion engines indicated that these compounds may be ubiquitous in combustion processes.

Other Sources

Soot from fireplaces. The carbonaceous material on the walls of the metal firebox of a 25-year-old fireplace, whose flue had not been cleaned for 10 years, was sampled in a manner designed to avoid contamination. Birch, oak, willow, mountain ash, and applewood untreated with preservatives had been burned in this fireplace, along with some paper to start the fire. The residue on firebrick in a 12-year-old fireplace, whose chimney had never been cleaned, was also sampled. The fuel had been hardwood, mostly oak, none of it treated with any wood preservatives. These samples were analyzed as described for mufflers. The results are presented in Table 3.

Particulates from a home electrostatic precipitator. Particulate material was collected from a home electrostatic precipitator. The collection represents the material accumulated during six spring and summer months of operation of the precipitator. The results obtained are also reported in Table 3.

Charcoal-broiled steaks. New York strip steaks grilled over a charcoal fire were sampled at 13, 18, and 28 minutes. Grilling for these times produced rare, well-done, and overdone samples. Each of the three samples was immediately wrapped in aluminum foil, placed in a plastic bag, and then put in a freezer to await analysis. Analyses were performed by method ML-AM-78-63. The results are shown in Table 3.

Cigarette smoke. Smoke generated by the simulated smoking of cigarettes (an arbitrarily selected national brand without filters) was analyzed for trace levels of chlorinated dioxins. The smoke was collected on special collection matrices consisting of 100/120-mesh silica (coated in situ with 20 percent hexadecane by weight) contained in a disposable glass transfer pipette. The cigarette was attached to the pipette by cleaned latex rubber tubing and puffed by applying gentle vacuum with a rubber pipette bulb. Approximately 20 to 30 puffs nominally 2 to 3 seconds in duration were collected from each cigarette. An entire package of 20 cigarettes was combusted during each experiment. Combustion experiments were conducted in two different urban locations. Before use, the inlet end of each collection tube was spiked with 2.0 nanograms of ^{13}C-labeled 2,3,7,8-TCDD, which served as an internal standard for TCDD quantitation after residue cleanup. Each collection tube was extracted with hexane, followed by a multistep cleanup, including reverse phase LC, to remove interferences. The LC eluent was subjected to both low-resolution GC-MS and electron capture GC analysis. The results are given in Table 3.

The further discovery that chlorinated dibenzo-*p*-dioxins are the result of commonplace burning involving fireplaces, charcoal broilers, and cigarettes supports the conclusion that these compounds may be ubiquitous in combustion processes.

Other Chlorinated Compounds Identified

The following compounds were identified in many of the samples: hexa-, hepta-, and octachlorodibenzofurans, decachlorobiphenyl, and polychlorinated terphenyls. Since analytical standards were not available and recoveries are not known, no quantitative measurements were made. These observations are in Table 5. The samples also contained numerous unknowns that were not qualitatively identified.

Waterborne particulates from scrubbers. Composite scrubber water samples were taken from the rotary kiln incinerator during the sampling reported in Table 4. The particulate matter was separated by filtration and the chlorinated dioxins were determined by analytical method ML-AM-78-63; the results are reported in Table 6. The water filtrate from the scrubber water composite was also analyzed and the results are shown in Table 6. The data from Table 6 together with the relative weight of scrubber water show that more than 99.7 percent of the chlorinated dioxins are associated with filterable particulate matter.

Conclusions

The following conclusions are supported by this study:

1) Some refuse incinerators and fossil-fueled powerhouses are sources of airborne and waterborne particulates that contain chlorinated dioxins.

2) Some gasoline- and diesel-fueled automobiles and trucks are sources of airborne particulates that contain chlorinated dioxins.

3) Some fireplaces, charcoal grills, and cigarettes have been identified as sources of particulate matter that contains chlorinated dioxins.

4) Chlorinated dioxins enter the environment by way of airborne particulate matter from combustion sources and waterborne particulate matter from scrubbers, which are increasingly required for major combustion sources.

5) Additional chlorinated compounds were observed and apparently arise from combustion; they include chlorinated dibenzofurans, decachlorobiphenyl, polychlorinated terphenyls, and others that have not been identified.

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16. Analytical method ML-AM-73-97 consists of a base digestion, an acid wash of the hexane extract, and cleanup with alumina and silica gel columns. Measurements are made by low-resolution GC-MS.
17. Analytical method ML-AM-78-63 includes Soxhlet extraction through a silica gel bed followed by cleanup through beds of silica, silver nitrate-modified silica, and basic alumina. Various chlorinated dioxins are separated by high-pressure liquid chromatography and measured by low-resolution GC-MS.
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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

DATE: August 8, 1978

SUBJECT: Interim Status Report 8EHQ-0778-0209

FROM: Frank D. Kover Charles M. Auer for FDK
Assessment Division, OTE/OTS

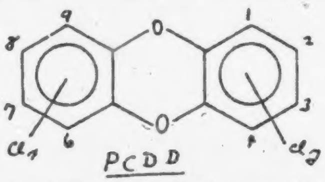
TO: Joseph J. Merenda, Director
Assessment Division, OTE/OTS

Approved J.J. Merenda 8/8/78

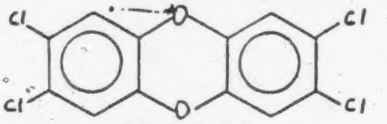
Revision
Needed ____________

APPENDIX (8EHQ-1178-0209) (Supplement)

The polychlorinated dibenzo-p-dioxins (PCDDs) are a series of tricyclic aromatic compounds which exhibit similar chemical and physical properties. The basic structure of PCDDs (as shown below) has eight possible points of chlorine substitution. From the monochloro to the octachloro derivatives, a total of 75 different positional isomers is possible.



PCDD



2,3,7,8-TCDD

The most extensively studied isomer of the PCDDs is 2,3,7,8-tetrachloro dibenzo-p-dioxin (2,3,7,8-TCDD), one of the most potent toxins presently known. The toxic effects induced by other TCDD isomers are less well characterized; however, they appear to exhibit a lesser degree of toxicity (both quantitatively and qualitatively) than 2,3,7,8-TCDD. For these reasons, the PCDD isomer attracting the greatest amount of Agency interest and activity is 2,3,7,8-TCDD.

Submission Evaluation (The following sections refer to subheadings in Dow's report.)

I. Building Blocks for Chlorinated Dioxins

The report's conclusions state that "conditions in a flame favor the occurrence of every conceivable type of chemical reaction" (p. 5), so that PCDDs may be formed in trace quantities wherever combustion occurs. The formation of polycyclic organic compounds during combustion is not a new finding. During coal combustion, the initial pyrolytic reaction can result in fragmentation, ring closures, condensation, and aromatization. The main products tend to be polynuclear ring compounds, occasionally containing nitrogen, oxygen, or sulfur, and simple compounds like H_2, H_2S, NH_3, CH_4, CO_2, etc.

Dow opens the discussion in Part I by establishing that inorganic chloride, gaseous products (SO_2, NO_x, CO, etc.), metals (V, Fe, Ni, etc.), and a wide variety of aliphatic and aromatic hydrocarbons are present during refuse- or fossil-fueled combustion reactions. The submitter then postulates that "at ultratrace levels, parts per billion, the number of compounds which may possibly form on particulate matter approaches or exceeds that presently known to man." While this statement may be true, it is never linked experimentally in Dow's submission to a demonstration that PCDDs will typically form during combustion reactions. Several authors (e.g., Buser *et al.* [*Chemosphere*, 7(2), 165, 1978]; Rappe *et al.* [*Chemosphere*, 7(3), 269, 1978], Stehl and Lamparski [*Science*, 196, 1008, 1977]; Ahling *et al.* [*Chemosphere*, 6(8), 461, 1977]; Buser and Rappe [*Chemosphere*, 7(2), 199, 1978]), on the other hand, have demonstrated in a laboratory setting that PCDDs can be formed during the pyrolysis of polychlorophenates (sodium salt) or polychlorophenoxy-containing materials (e.g., polychlorophenate-impregnated leaves, wood shavings, plywood, or waste oil). Rappe *et al.* (1978) stated that the concentration of PCDDs in the combusted samples represented a sizeable increase over the levels detected in the original polychlorophenate samples.

IV. Airborne Particulate Matter

Soil samples were collected from "13 different locations inside and outside (Dow's) Midland Plant" and analyzed for tetrachlorodibenzo-p-dioxin (TCDD), hexachlorodibenzo-p-dioxin (HxCDD), heptachlorodibenzo-p-dioxin (HpCDD), and octachlorodibenzo-p-dioxin (OCDD). Dow does not further identify the sites with respect to individual locations or distances from the plant or specific plant operations. The analytical results are presented in Table 1. Dow notes that the analytical method was not validated and, therefore, the results are qualitative only.

Table 1. PCDDs in 13 Midland Soil Samples[a] (taken from p.17 of Dow's report)

TCDD	HxCDD	HpCDD	OCDD
4/13	9/13	13/13	13/13

a) Collected from "inside and outside the Midland plant."

A second set of soil samples was collected in the same manner; 5 of these, "including the ones corresponding to those that previously gave positive TCDD results, were analyzed by a newly developed and validated analytical method." Dow goes on to state that this new method permitted the separation of the 2,3,7,8-TCDD from "almost all of its other 21 isomers." These results are summarized in Table 2. The specific sample selection sites represented by Table 2 should be clearly identified as to their placement with respect to the Dow plant.

Dow's claim at this juncture and at subsequent points in the submission that its analytical method permitted separation of TCDD isomers is not adequately supported by any of the figures shown in the submission or the attached appendices. Dow should be asked to provide a detailed description of the methods of extraction and analysis as well as the criteria utilized in the identification of TCDD isomers; e.g., (a) GC/HRMS (gas chromatography/high resolution mass spectroscopy) detection method, (b) elemental composition of molecular masses m/e 320, m/e 322, and m/e 324, (c) molecular ion Cl ratio, 0.8/1.0, (d) GC/HRMS retention time of test samples and confirmatory samples fortified with specific TCDD isomers, (e) m^+ - COCl loss, m/e 257, (f) use of and techniques for GC/HRMS double ion monitoring, (g) a description of the capillary column GC resolution measured in theoretical and/or effective plates, and (h) a description of the degree of GC resolution of specific TCDD isomers (Dow's tables should be more specific and indicate identified isomers and their contribution to the total value shown). In addition, Dow should clarify if the quantified values of TCDD isomers shown in its report are based on the response of specific isomers or if the values are normalized to the response of 2,3,7,8-TCDD. Finally, there is some question that the harsh (acid) conditions used for sample extractions may have resulted in PCDD formation from precursers or by dechlorination of higher PCDD isomers. Dow should be asked to confirm its findings by providing comparative results from neutral extraction procedures, if available.

The information needs outlined in the preceding paragraph concerning TCDD isomer values also apply in all cases to HxCDD, HpCDD, and OCDD isomer values reported in the Dow submission. Any available data on the presence of pentachloro dibenzo-p-dioxin isomers in environmental samples should also be requested.

Dow states on p.2 of its report that the "analytical methodology is so very new that it has not always been validated and not yet corroborated by other scientists." Limited analytical significance can be derived from results generated using nonvalidated procedures. In order to derive significant and valid analytical meaning and/or conclusions from the results of part per billion (ppb) and part per trillion (ppt) analysis for PCDDs, the results must be accompanied by (1) appropriate quality control results and (2) a complete description of the criteria utilized to identify and confirm the presence of PCDD residues. Furthermore, in cases where the reported PCDD residue levels and the limit of detection are of identical or approximately equal value, such numbers have uncertain analytical significance especially in situations when nonvalidated analytical methods are employed. PCDD values which are not greater than ten times (10X) the noise have been identified with an asterisk (*) in this status report. (When analyzing for trace levels of PCDDs, a signal to noise ratio of 2.5:1 is considered to be the level of detection; values below this ratio are reported as non-detected [ND]. When a sufficient amount of the sample and time are available to the analytical chemist, samples having a signal to noise ratio between 2.5:1 and 10:1 should be rerun a second time to verify the result. If the second analysis falls between 2.5:1 and 10:1, the two separate results and the average should be reported. Values resulting from a single analysis are not contested if the signal to noise ratio is at least 10:1 and the ratio of peak heights m/e 322:m/e 320 is in the proper isotopic proportion.)

Table 2. PCDDs in 5 Midland Soil Samples[a] (ppb)
(taken from Dow's Table III)

Sample	TCDD isomers other than 2,3,7,8-TCDD	2,3,7,8-TCDD[b]	HxCDD	HpCDD	OCDD
1	17	16	280	3200	20500
2	9	6	40	470	2500
3	18	100	120	650	6300
4	18	16	280	240	11700
5	0.8	0.3	7	70	490

Note:

a) Taken from "inside and outside the Midland plant."

b) Values are reportedly based on the "separation of the 2,3,7,8-TCDD from almost all of its 21 other isomers" (see discussion in the text).

Next, dust samples were collected at various locations in a "Dow research building" and subsequently extracted and analyzed using a method reportedly separating "the 2,3,7,8-TCDD from all but about 11 of its isomers". (As discussed earlier, this statement should be supported by documentation indicating that eleven TCDD isomers plus the 2,3,7,8-TCDD equals one fraction. Dow's statement to that effect is not sufficient.) The results of this work are presented in Table 3. Dow should be asked to clearly describe what it means by the term "air intake." Does the PCDD contamination of this air intake dust result from the handling of "inside" or "outside" air?

Table 3. Dust Samples from a Dow Research Building (ppb) (taken from Dow's Table IV)

Sample	TCDD isomers other than 2,3,7,8-TCDD	2,3,7,8-TCDD[a]	HxCDD	HpCDD	OCDD
1st floor	0.5	1.0	18*	240*	960
1st floor	2.3	2.3	28	520	3800
2nd floor	1.3	2.6	11*	140	650
2nd floor	-	0.7	9*	250	2600
2nd floor (2 weeks after cleaning)	1.5	1.2	20*	320	2000
air intake	2.3	2.3	35*	1200	7500

a) Values are reportedly based on the "separation of the 2,3,7,8-TCDD from all but about eleven of its isomers" (see discussion in the text).

*Value is close to the detection limit for the analytical method employed (signal is less than 10X noise).

Additional dust samples from Midland and an unspecified "metropolitan area" were collected and analyzed for control purposes. These samples did not satisfy this need, therefore, dust and soil samples were collected from additional, vaguely characterized ("rural," "urban," and "major metro") sites. Table 4 represents a composite presentation of these results.

Dow concludes (p.21) that these data (Tables 1-4) "strongly support the conclusion that chlorinated dioxins are produced in incinerators and fossil fueled powerhouses as a consequence of combustion. These results indicate that chlorinated dioxins are more widespread than previously anticipated and are perhaps ubiquitous". In point of fact, the results presented offer no scientific documentation (other than weakly circumstantial evidence) relating Dow's observations on PCDD contamination of soil and dust to the synthesis of PCDDs as a by-product of incineration or power generation. There is some circumstantial evidence that the HxCDD, HpCDD, and OCDD identified in the soil samples from the urban and the metropolitan areas may be associated with the operation of a powerplant and an incinerator, respectively. This, however, does not demonstrate that the presence of these substances results from their synthesis as a normal combustion by-product. Table 5 presents a comparison of the total number of PCDD-positive samples collected from the Midland, MI area with those collected from other locations. From Table 5, the following observations, contrasting Dow's claims, can be supported:

a) Midland, MI, and especially the area around the Dow plant, exhibits the greatest evidence for gross PCDD contamination among the various locations sampled. This is true both in terms of the proportion of samples in which PCDDs were detected and the degree of contamination evident in individual samples. In the latter case, the levels of PCDDs found in Midland are 2-4 orders of magnitude greater than those reported at other locations. The fact that much higher levels of PCDDs were found in the soil and dust around the Dow chemical plant as compared to urban, metropolitan, and rural areas suggests that polychlorophenol production or some other activity (spills, plant emissions, combustion of chemical wastes, etc.) at the Dow plant may be the source of the observed PCDD contamination.

(b) To the extent that TCDDs, especially 2,3,7,8-TCDD, are the PCDDs of greatest Agency concern, the levels of TCDDs identified in Midland soil and dust samples indicate that this area represents a definite TCDD "hot spot." In comparison, there are very few instances where TCDDs were reported at other sites.

V. Incineration

In its introduction to this section, Dow cites several European authors who have reported the presence of PCDDs in fly ash and flue gas from municipal incinerators (Olie *et al.*, *Chemosphere*, 6(8), 455, 1977), in fly ash alone from a municipal incinerator, and in fly ash from an industrial heating facility (Buser *et al.*, *Chemosphere*, 7(2), 165, 1978). Dow notes (p.22) that Olie *et al.* postulate that the PCDDs are formed as a result of the thermal condensation of chlorophenols, although mention is made in the article that a thermal synthesis reaction involving inorganic chloride and organic material (especially hexachlorobenzene and other highly chlorinated benzene) "was considered to be entirely possible." Dow, however, fails to discuss aspects of the Buser *et al.* (1978) study as well as a Rappe *et al.* (*Chemosphere*, 7(3), 269, 1978) study which indicate that the pattern of PCDD isomers identified in fly ash (from incinerators and heating facilities) was almost identical to that found when a mixture of polychlorophenates was pyrolyzed under controlled conditions. Buser *et al.* go on to state

Table 4. PCDDs in Soil and Dust Samples (ppb)
(taken from Dow's Tables III, IV, V, and VI)

Sample	TCDD	HxCDD	HpCDD	OCDD
Midland				
(1)	0.03*	0.2	2.3	19
(2)	0.04*	0.4	3.9	31
(3)	See Tables 2 and 3 for other Midland values.			
Rural				
(1)	ND	ND	ND	ND
(2)	ND	ND	ND	0.1*
(3)	ND	ND	ND	ND
(4)	ND	ND	0.3*	0.10
(5)	ND	ND	0.05*	0.17
(6)	ND	ND	0.02*	0.16
(7)	ND	ND	ND	ND
(8)	ND	ND	0.03*	0.11*
Urban[a]				
(1)	ND	1.2	1.6	2.0
(2)	ND	ND	0.23	0.96
(3)	ND	0.03*	0.30	2.0
(4)	ND	ND	ND	0.05*
(5)	ND	ND	0.035*	0.20
Major Metro[b]				
(1)	ND	ND	0.14	0.41
(2)	ND	0.03*	0.24	1.0*
(3)	0.03	0.31	3.3	22.0
(4)	ND	0.12*	1.4	8.5
(5)	0.006*	0.14	0.85	3.2
(6)	0.005*	0.04*	0.36	1.4
(7)	0.005*	0.09*	0.96	6.0
(8)	ND	0.02*	0.10	0.35
(9)	ND	ND	0.64	2.6
(10)	0.04*	0.34*	3.2	8.2
(11)	ND	0.09	0.8	3.5
(12)	ND	0.1	0.3	0.4
(13)	ND	ND	ND	ND
(14)	ND	0.3	1.0	3.8

a) Samples collected from between 300-1500 feet from a "powerhouse."

b) Samples collected from between 100-3300 feet from an "incinerator" (except for (14) which was collected at a "metro river shoreline").

*Value is close to the detection limit for the analytical method employed (signal is less than 10X noise).

ND) Signal not detected at 2.5X noise.

Table 5. A Comparison of PCDD-Positive Soil and Dust Samples/ Total Analyzed from Different Locations

Location	TCDD Isomers	2,3,7,8-TCDD	HxCDD	HpCDD	OCDD
Midland, MI	16/25[a] (64%)[b] (0.03-10)[c]	11/11[d] (100%) (0.3-100)	22/26 (88%) (0.2-280)	26/26 (100%) (2.3-3200)	26/26 (100%) (19-20500)
Other Locations (total)	5/23 (22%) (0.005-0.04)		10/23 (43%) (0.02-1.2)	18/23 (78%) (0.02-3.3)	20/23 (87%) (0.05-22.0)
Rural	0/8 (0%)		0/8 (0%)	4/8 (50%)	5/8 (63%)
Urban	0/5 (0%)		2/5 (40%) (0.03-1.2)	4/5 (80%) (0.035-1.6)	5/5 (100%) (0.05-2.0)
Major Metro	5/10 (50%) (0.005-0.04)		8/10 (80%) (0.02-0.34)	10/10 (100%) (0.10-3.3)	10/10 (100%) (0.35-22.0)

a) This entry reportedly represents TCDD isomers other than 2,3,7,8-TCDD; i.e., the analytical method is claimed to have achieved some degree of TCDD isomer separation. All other entries in this column apparently represent aggregate totals for all TCDD isomers.

b) Percent (PCDD-positive samples/location). Note that for purposes of this table, asterisked (*) values taken from Tables 3 and 4 were considered "positive" despite questions as to the analytical significance of some of these values.

c) Range of detected levels in ppb.

d) This entry reportedly represents some degree of separation of the 2,3,7,8-TCDD from other TCDD isomers.

that available evidence indicates that commercial chlorophenols cannot be excluded as the precursor to PCDDs in fly ash. As noted briefly in the dicussion of part I, Rappe et al. (among others) have also shown that the combustion of leaves, wood shavings, plywood, or waste oil containing chlorophenates can yield a variety of PCDD isomers in the ash. Dow reports that it operates two major chemical waste incinerators at Midland, MI. The first is a large stationary tar burner and the second is a rotary kiln incinerator. Samples of particulate matter were removed from the stacks and analyzed for PCDDs. The resulting data are summarized in Table 6. Particulates from the stationary tar burner and the rotary kiln incinerator show no detectable TCDD when operated with supplementary fuel. (The levels of the other PCDD isomers are, nonetheless, still relatively high.) However, when the rotary kiln incinerator is operated without supplemental fuel, extremely high levels of TCDDs (and other PCDDs as well) are detected. Several important questions immediately arise. Does Dow generally operate the rotary kiln incinerator with supplemental fuel when using it for chemical waste incineration? Dow should specify the types and conditions of operation of air pollution control devices (including scrubbers) used to control particulate emissions from these incinerators? It is also important to know whether the particulate samples were collected from the stacks "upstream" or "downstream" from the scrub water inlet (i.e., before or after scrubbing) (see part VII below). In addition, were the particulates scraped from the walls of the stacks or were they collected from the gas phase or an electrostatic precipitator (or some other pollution control device).

VI. Powerhouses

Particulates from a Dow Midland powerhouse stack were collected and analyzed. Fuel oil and coal are burned in the powerhouse. The results of the PCDD analyses are presented in Table 7.

It is not clear why the TCDD isomers (other than 2,3,7,8-TCDD which was not detected) are so high (compared to other PCDDs) in the powerhouse particulate. Likewise, if Dow's thesis concerning the synthesis of PCDDs as a normal combustion by-product is correct, why do the incinerators as opposed to the powerhouse, in general, show higher levels of PCDDs in the fly ash? The difference may be related to the nature of the material being burned in each operation. One possible explanation is that the chemical wastes being burned in the incinerators already contain PCDDs or PCDD precursors (polychlorophenoxy material); that is, the wastes

Table 6. PCDDs in Particulate Matter from Dow Incinerators (ppb) (taken from Dow's Tables VIII and IX)

Sample	TCDD isomers other than 2,3,7,8-TCDD	2,3,7,8-TCDD[a]	HxCDD	HpCDD	OCDD
	Stationary tar burner (with supplemental fuel)				
(1)	ND	ND	20	90	330
(2)	ND	ND	7	125	440
(3)	ND	ND	6	60	190
(4)	ND	ND	4	160	320
(5)	ND	ND	1	27	250
	Rotary kiln incinerator (without supplemental fuel)				
(1)	1,800	2,800[b]	13,000	110,000	180,000
(2)	5,000	8,200[b]	65,000	510,000	810,000
(3)	3,300	110	1,300	2,000	3,000
(4)	12,000	ND	5,600	37,000	59,000
	Rotary kiln incinerator (with supplemental fuel)				
(1)	ND	ND	1.4	13.0	30.0
(2)	ND	ND	ND	4.0	9.0
(3)	ND	ND	ND	6.0	15.0
(4)	ND	ND	5.0	27.0	170.0
(5)	ND	ND	4.0	110.0	950.0

a) Dow's report does not specify the number of TCDD isomers represented by values in this column.

b) These values may be high; see Dow's comment on p.24.

Table 7. PCDDs in Particulates from a Powerhouse Stack (ppb) (taken from Dow's Table X)

TCDD isomers other than 2,3,7,8-TCDD	2,3,7,8-TCDD[a]	HxCDD	HpCDD	OCDD
38*	ND	2	4	24

a) Dow's report does not specify the number of TCDD isomers represented by this value.

*Value is close to the detection limit for the analytical method employed (signal is less than 10X noise).

result from Dow's chlorophenol production processes. Rappe et al. (1978) offer several different mechanisms for the formation of PCDDs given the presence of pre-formed PCDDs or PCDD precursors. The 3 proposed mechanisms are:

a) by dimerization of chlorophenates,

b) by dechlorination of higher chlorinated PCDDs, and

c) by cyclization of PCDD precursors.

VII. Waterborne Particulates

Composite scrubber water samples were taken from the rotary kiln incinerator during the same sampling reported in part V of the report. Particulates were filtered from the scrubber water and both the particulates and the water filtrate were analyzed for PCDDs. (Note that Dow's analytical method ML-AM-78-63 [Dow's Appendix B3] [specific for soil, dust, and particulate samples] was used to analyze the scrubber water particulates. Dow, however, does not specify the analytical method used to examine the water filtrate. This should be clarified.) Table 8 presents the results of these analyses and also compares the scrubber water PCDD values with those reported for rotary kiln fly ash (previously reported in Table 6). When comparing the PCDD levels reported in the different samples, it should be noted that there is no indication whether all the samples were taken within a short time of each other or days apart. In addition, it is not clear if the same wastes were being burned or if similar incineration conditions existed when the respective samples were taken. Dow should be asked to provide a complete description of the operating conditions (normally and during sampling), nature of the wastes burned normally and during sampling, and use of air pollution control devices on the rotary kiln incinerator. Dow should also describe the method of disposal used for scrubber water particulates and any other solid wastes resulting from these incineration procedures.

In addition, Dow should provide the same information for its stationary tar burner.

VIII. Combustion of Dioxins

The U.S. EPA report entitled "At-Sea Incineration of Herbicide Orange Onboard the M/T Vulcanus" (EPA-600/2-78-086) was published in April, 1978. A copy of this publication should be transmitted to Dow in any followup to this submission.

Table 8. PCDDs in Rotary Kiln Scrubber Water and Stack Fly Ash (ppb)
(taken from Dow's Tables IX, XI, and XII)

Without supplemental fuel

Sample	TCDD isomers other than 2,3,7,8-TCDD	2,3,7,8-TCDD	HxCDD	HpCDD	OCDD
A) scrubber water particulates	300	2,200[a]	3,400	26,000	42,000
B) scrubber water filtrate	0.0018*	0.001[a]*	0.005	0.24	0.026
C) fly ash particulates[b] (1)	1,800	2,800	13,000	110,000	180,000
(2)	5,000	8,200	65,000	510,000	810,000
(3)	3,300	110	1,300	2,000	3,000
(4)	12,000	ND	5,600	37,000	59,000
With supplemental fuel					
D) scrubber water particulates	14	32[a]	200	970	1,200
E) fly ash particulates[b] (1)	ND	ND	1.4	13.0	30.0
(2)	ND	ND	ND	4.0	9.0
(3)	ND	ND	ND	6.0	15.0
(4)	ND	ND	5.0	27.0	170.0
(5)	ND	ND	4.0	110.0	950.0

a) The analytical method reportedly did not separate the 2,3,7,8-TCDD from 11 other isomers.

b) The high results reported for 2,3,7,8-TCDD "are probably due to analysis by the non-specific GC-MS packed column method" (see p.24 of Dow's report). In addition, Dow's report does not specify the number of TCDD isomers represented by the values in the 2,3,7,8-TCDD column.

*Value is close to the detection limit for the analytical method employed (signal is less than 10X noise).

IX. Michigan Division Manufacturing Plants as Potential Sources of Trace Levels of Chlorinated Dioxins in the Environment

A. Wipe testing

The fact that 8 out of 230 wipe tests gave positive results for TCDD merits consideration. The wipe test area, 100 cm^2, is roughly equivalent to the area of a human hand and 1 ug TCDD may be approaching a toxic level (LD_{50} male guinea pig, 0.6 ug/kg). The text indicates that the analyses were conducted by gas chromatography with a detection limit of 1 ug/wipe; however, Appendix B4 states that analyses were carried out by GC-MS with a level of detection of 0.1 ug/sample. These points should be clarified. In addition, information as to the suitability of the wipe test methodology to actual conditions which might be encountered in the Michigan Division manufacturing plants should be provided by Dow.

B. Air monitoring

The method of sample collection is not described in sufficient detail in Dow's report. Are particulates sampled during this procedure? Also, note that part of the report appears to have been omitted at the top of page 30. This omission should be clarified.

A statement made on p.30 could be misleading. "The few molecules that take this path (vaporization) will be destroyed by photodegradation within a few hours even when the day is cloudy (23)." This statement could lead one to believe that if PCDDs are released to the atmosphere they will be destroyed. If these compounds are really volatilized then they could possibly be decomposed; however, if they are adsorbed onto fly ash or other particulate matter they would probably not be destroyed photolytically or to only a limited extent. In addition, the applicability of Dow's reference 23 (Nash and Beall, 1977) to the above quotation is not clear; clarification is required.

Dow claims on page 30 that the "wipe testing and air monitoring data are strong evidence that (Dow) manufacturing plants do not emit levels of chlorinated dioxins sufficient to explain the finding of these compounds in the soil samples reported earlier." No scientific basis for this conclusion is provided in the data presented by Dow. In the first place, there is no way to compare the ppb levels of TCDD found in soil and dust with the "1 ug/wipe" values reported for the wipe testing. To support its conclusion, Dow would either have to "wipe test" soil samples or, preferably, analyze pesticide plant wipes on a ng/g (ppb) basis. Handled in any other way, one is left to compare apples with oranges. Similarly, there is no way to compare Dow's plant air monitoring data with the PCDD values reported for soil and dust samples collected outside the plant. Furthermore, there is no indication as to the location of each wipe test or air sampling site in relation to the various operations involved with polychlorophenol production or handling. Dow should present a grid of its polychlorophenol production and handling sites and identify the sampling points for the 230 wipe tests and 35 air monitoring assays. Any available monitoring data (wipe tests, air sampling, etc.) regarding Dow laboratory facilities as potential sources of PCDD contamination should also be provided.

C. Aqueous streams

Further information on the "tests" for primary organics reported in this section should be provided by Dow.

D. Cooling waters

The results of Dow's analyses of cooling tower "residues" for PCDDs are shown in Table 9. It is important to know if these towers cool steam or other effluent streams from the polychlorophenol facilities, the power plants, or the incinerators discussed earlier. Dow should provide a map of its plant site showing the location and relationship of each cooling tower, incinerator, powerhouse, and production facility (especially those producing or handling polychlorophenols or derivatives). In addition, Dow should further describe what it means by "cooling tower residue"; is this a water or sediment sample? Dow should also support with analytical results its statement on page 30 that "product leaks to cooling towers" do not occur.

Table 9. PCDDs in Cooling Tower Residues (taken from Dow's Table XIII)

Location	TCDD	HxCDD	HpCDD	OCDD
Northwest	ND (L.O.D.[a] 0.05)	ND	25	119
East	ND (L.O.D. 0.05)	ND	12	56
Central #1	1.6*	10	20	107
Central #2	6.0	-	-	-

a) Level of detection was 0.05 ppb.

*Value is close to the detection limit for the analytical method employed (signal is less than 10X noise).

Dow states in this section (p.30) that "(it) was assumed that cooling tower residues would be positive for chlorinated dioxins." Dow should be asked to provide the basis for this assumption. On page 31, Dow states that "(from) these data (see Table 9), we conclude that the presence of chlorinated dioxins in cooling tower residues confirms the airborne route." Dow should be asked to explain the term "airborne route" and specify the sources of the PCDDs found in cooling tower residues.

Central to this discussion of cooling towers is the assumption that Dow does not use 2,4,5-trichlorophenol in its cooling tower waters as a biocide. Dow should be asked to clarify this point. In the event that Dow does use 2,4,5-trichlorophenol, then the PCDDs found in the cooling tower residues may not be from airborne particulates.

E. Various aqueous streams

For this part of the report, Dow sampled various aqueous streams in its Midland plant. The samples were collected from sewer lines before they entered the waste treatment plant. The samples were selected on the basis of "the stream source and its rate of flow." This vague description of the samples is inadequate. Do any of the sampled aqueous streams come directly from chlorophenol production or handling operations? Do these samples include particulates? If not, these analyses have limited value. Dow indicates it employed analytical method ML-AM-73-97 (Appendix B2) for the analyses reported in this section. The method is specified for the analysis of fish and soil samples; its applicability to aqueous stream analysis should be demonstrated.

On page 32, Dow states that in the case of sewer water analyses, "the source of the chlorinated dioxins cannot be reliably determined by the ratio of the various species." However, in immediate juxtaposition to this statement is Dow's remark (p.33) that "(with) the exception of sewer water samples 2 and 4 and cooling tower central #1, the data indicate that the chlorinated dioxins are from the same source as those on soil and dust. The exceptions have species whose ratios are similar to those found on particulates from the powerhouse." Dow should clarify the meaning and significance of these remarks. Insofar as Dow states in the Introduction (p.2) that "(samples) were not taken by statistical design and results are not intended to represent anything other than the sample analyzed," how can Dow proceed to compare the PCDD ratios from one sample with those from another? Moreover, how can Dow draw conclusions from such a comparison? Furthermore, how can the submitter state in one paragraph that a comparison of PCDD ratios will not yield a "reliable" determination of the source, but then in the next paragraph draw 2 separate and distinct conclusions from these same ratios.

Another statement on page 33 deserves comment: "The (PCDD) ratios (found in the cooling tower or sewer waters) do not fit those normally found in any manufactured product." The meaning of the phrase "normally found in any manufactured product" is not clear because no known polychlorophenol product or derivative contains both TCDD and OCDD. In general, trichlorophenol contains TCDD, while pentachlorophenol contains HxCDD, HpCDD, and OCDD but no TCDD. If Dow is aware that any of its products contain both TCDD and OCDD (or for that matter, both trichlorophenol and pentachlorophenol), it should so inform the Agency. Dow should describe the spatial relationship of its trichlorophenol production facility to the location of its pentachlorophenol production site. Are any waste water lines common to both? What is the composition of the chlorophenol wastes incinerated by Dow? Do these wastes represent a composite of both trichlorophenol and pentachlorophenol wastes? Or are wastes from the two chlorophenol production processes burned sequentially in the same incinerator?

X. Chlorinated-dioxin Containing Particulate Matter from Mufflers

Dow reports trace quantities of PCDDs in scrapings taken from the inside of car and diesel truck mufflers. The cars sampled were equipped with and without catalytic converters. Does this necessarily mean, as Dow advances, that PCDDs are formed during combustion in the engine? If the car or truck was driven primarily in an industrial area or near sources that might be considered contaminated with PCDDs or PCDD precursors, airborne particulates containing these substances could be drawn into the air intake of the engine. Any PCDDs not decomposed in passage through the engine might then be deposited in the muffler. The statement (p.35) that PCDDs "are in particulate emissions from internal combustion engines" cannot be supported because vehicles' exhaust gases were not analyzed. The only conclusions that can be supported by the observations presented in this section are that (1) PCDDs have been identified in some muffler scrapings, however, (2) the source of the PCDDs is unknown.

The analytical method (GC-EC vs. GC-MS) used to detect TCDD isomers was not specified in Dow's Table XV; this information should be provided.

XI. Commonplace Sources

1. Soot from fireplaces

Dow reports that soot collected from 2 fireplaces contains PCDDs. The results are presented in Table 10. Dow states (pp. 35 and 36) that none of the wood burned in the fireplaces "had been treated with any wood preservatives." Dow should be asked to document this statement.

2. Particulate matter from a home electrostatic precipitator

The results of PCDD analysis performed on this sample are presented in Table 10.

Table 10. PCDDs in Fireplace Soot and Particulates from a Home Electrostatic Precipitator (ppb) (taken from Dow's Table XVI)

Source	TCDD isomers other than 2,3,7,8-TCDD	2,3,7,8-TCDD[a]	HxCDD	HpCDD	OCDD
fireplace A	0.27	0.1*	3.4	16	25
fireplace B	ND	ND	0.23	0.67	0.89
electrostatic precipitator	0.40*	0.6*	34	430	1300

a) Dow's report does not specify the number of TCDD isomers represented by values in this column.

*Value is close to the detection limit for the analytical method employed (signal is less than 10X noise).

The geographic location of each house sampled in Table 9 should be provided by Dow. Were these houses in the Midland, MI area, and if so were they near Dow's plant? This is of some interest because the particulate collected in the electrostatic precipitator (electronic air cleaner) have a higher concentration of PCDDs than the soot samples from the fireplaces (acknowledged sources of typical combustion by-products). A home electrostatic precipitator functions to a certain extent as a "high volume air sampler." In the case cited by Dow, the electrostatic precipitator was operated over a period of 6 spring and summer months. Thus, the precipitator particulates analyzed by Dow represent airborne material collected over a 6 month period which does not coincide with the months generally associated with heavy space heating-related combustion or home fireplace usage. Therefore, the PCDD values for the home electrostatic precipitator-collected particulates may, to a certain extent, represent the results of incidental ambient air "sampling" conducted at the site of the house. For this reason, the location of this particular house may be important.

3. Charcoal broiled steaks

The results of this assay are presented in Table 11. As can be seen, all samples were negative for TCDD and HxCDD and in only one case (that being an "over-done" steak) did the GC-MS (gas chromatography-mass spectrometry) method of analysis "support" the GC-EC (gas chromatography-electron capture) result. However, even in that case (as in all other instances reported in the table), the reported OCDD residues and the level of detection are of identical or approximately equal value such that the number has limited analytical significance. Furthermore, the blank sample (uncooked steak?) had a concentration of 6 ppt of OCDD (determined by GC-EC, although the value is so close to its level of detection as to have limited analytical significance). Was this blank (uncooked steak?) contaminated with pentachlorophenol, a widespread environmental contaminant?

Table 11. PCDD Content of Charcoal Grilled Steak (ppb)
(taken from Dow's Table XVII)

Sample	TCDD isomers other than 2,3,7,8-TCDD	2,3,7,8-TCDD	HxCDD	HpCDD		OCDD	
				GC-MS	EC	GC-MS	EC
blank	ND	ND	ND	ND	0.004*	ND	0.006*
medium-rare	ND	ND	ND	ND	0.003*	ND	0.005*
well-done	ND	ND	ND	ND	0.006*	ND	0.012*
over-done	ND	ND	ND	ND	0.007*	0.029*	0.016*

*Value is close to the detection limit for the analytical method employed (signal is less than 10X noise).

XII. Cigarette Smoke

Cigarette smoke particulates were also analyzed for PCDDs; the results are presented in Table 12.

Table 12. PCDDs in Cigarette Smoke Particulates
(10^{-12} g/cigarette)
(taken from Dow's Table XVIII)

Location of purchase and test	TCDD isomers other than 2,3,7,8-TCDD	2,3,7,8-TCDD[a]	HxCDD	HpCDD	OCDD
urban 1	ND	ND	8.0	8.5	50
urban 2	ND	ND	4.2	9.0	18

a) Dow's report does not specify the number of TCDD isomers represented by values in this column.

Several questions arise concerning this assay. Are PCDDs or PCDD precursors present in unburned cigarettes (possibly due to pesticide use of polychlorophenols or derivatives)? How does 10^{-12} g/cigarette relate to 10^{-12} g/g (or ppt)? The cigarettes were smoked in two unidentified "urban locations"; why was this method chosen over a controlled study conducted in a lab? Were the cigarettes "smoked" near Midland, MI or some other industrial site; in other words, how would the results of ambient air sampling at the two locations compare with the reported cigarette-PCDD values? Do the individual results in Dow's Table XVIII represent GC-EC or GC-MS analysis? Are the methods confirmatory in their results?

XIII. Other Chlorinated Compounds Identified

The polychlorinated dibenzofuran (PCDF) findings reported in this section should be investigated further. Several investigators (Buser *et al.*, *Chemosphere*, 7(5), 419, 1978a; Rappe *et al.*, *Chemosphere*, 7(5), 431, 1978; Buser *et al.*, *Chemosphere*, 7(5), 439, 1978b; Rappe *et al.*, *Chemosphere*, 6(5), 231, 1977; Buser *et al.*, *Chemosphere*, 7(1), 109, 1978c; etc.) have identified PCDFs in polychlorophenol pesticides, saw dust from polychlorophenol-treated wood, fly-ash, PCB mixtures, and as a by-product of the combustion of PCBs. Of significance are the Buser *et al.* (1978a) findings that the *major* PCDF constituents (*in fly* ash as well as in PCB pyrolyzates) tended to be the most toxic PCDF isomers (2,3,7,8-tetra-CDF; 1,2,3,7,8-penta-CDF; and 2,3,4,7,8-penta-CDF). This contrasts with the Buser *et al.* (1978a) findings on the distribution of PCDD isomers in polychlorophenate pyrolyzates where the less toxic isomers were in greatest concentration.

DIOXIN IN MIDLAND, MICHIGAN

1. The article "Trace Chemistries of Fire: A Source of Chlorinated Dioxins" was published in the October 24, 1980 issue of Science.

   A. Was this article written by Dow scientists?

   ANSWER: Yes

   B. Was the scientific data on the existance of dioxin in the Dow plant and in Midland, Michigan collected and analyzed by Dow scientists?

   ANSWER: Yes

DIOXIN LEVEL AT 100 parts per billion (ppb)

2. On page 387 of the article in "Table 3. Chlorinated dioxins in the environment," is a section on soil. In the soil section there is a line which reads "Dow Chemical (Midland, Michigan) 0.3 - 100 ppb." This is under the section 2,3,7,8-TCDD.

   A. This indicates that dioxin contamination is as high as 100 ppb. What is the exact location of the five samples in which dioxin contamination was found? Inside the Dow plant? in Midland?

   ANSWER: Dow recently received a request covering this information from the Michigan Department of Natural Resources, to which we have very recently responded. A copy of that response is enclosed (Exhibit A). Please note that we regard this as sensitive information, have treated it as confidential, and have asked MDNR to treat it appropriately. We trust you will do the same.

   B. How scientifically accurate was the analysis of these samples?

   ANSWER: To the best of our knowledge, it was the most accurate available at that time. However, the results were not specific to 2,3,7,8-TCDD. The numbers reported were totals for 2,3,7,8-TCDD plus 11 other isomers of dioxin.

   C. Has anyone other than Dow scientists ever analyzed the soil around the Dow plant for dioxin contamination?

   ANSWER: Not to my knowledge.

D. Would you object if EPA and the Center for Disease Control collected and analyzed soil samples around the plant?

ANSWER: As stated in our testimony of March 23, 1983, our concerns in such a dioxin study would be that a proper and meaningful protocol be used and that appropriate precautions be taken to protect any Dow proprietary information and technology within the plant. Assuming those concerns can be resolved (and we think they can) we would have no objection. In fact, on June 1, 1983, Dow announced several scientific initiatives, including a cooperative soil study covering these specific points. A copy of the information distributed with that announcement is included with these answers for your further information. (Exhibit B)

E. Has the Dow plant in Midland ever accidentally released dioxin contaminated chemicals into the environment? Specifically, did the Dow plant in Midland release dioxin contaminated chemicals such as 2,4,5-T into the environment in 1970?

ANSWER: We do not presently have this information available, however, in a request dated April 11, 1983, Region V of EPA requested extensive information regarding possible releases and possible sources of releases of dioxin from Dow's Midland manufacturing facilities. I immediately assigned a number of Dow personnel to collect the requested information and have supplied numerous documents to EPA in response. My best estimate at this time is that we will complete this process within two to three months.

OTHER DIOXINS IN THE ENVIRONMENT

3. In Table 3 of the article from Science, on the same line with Dow Chemical (Midland, Michigan) and under the column labeled OCDD (octa chlorinated dioxins) the levels of contamination range from 490 - 20,000 ppb.

NOTE: The following responses have been supplied by our Health & Environmental Sciences Department.

A. Compared to TCDD (dioxin), how toxic is OCDD?

ANSWER: Based on acute oral LD50's (See references (1) and (2) below):

- OCDD is 45 thousand (45,454) times less toxic than 2,3,7,8-TCDD to male rats.
- OCDD is 22 thousand (22,222) times less toxic than 2,3,7,8-TCDD to female rats.
- OCDD is 14 thousand (14,084) times less toxic than 2,3,7,8-TCDD to mice.

Please note the following additional points:

- OCDD is not teratogenic in rats at doses of 100,000 or 500,000 µg/kg/day.
- OCDD is not maternally toxic when given to pregnant rats in a teratology study at 500,000 or 100,000 µg/kg/day.
- TCDD (2,3,7,8) caused maternal and fetotoxicity to rats at doses of $\geq$ 0.125 µg/kg/day and was teratogenic to mice at doses of $\geq$ or 3 µg/kg/day.
- OCDD did not cause chloracne at a concentration >100,000 ppm compared to a (+) chloracne response to 2,3,7,8-TCDD at 0.04 ppm.

B. Is there any scientific evidence to substantiate the toxicity level of OCDD?

ANSWER: Yes, the scientific evidence has been published in references (1) (2) and (3), below.

C. How could OCDD harm human health?

ANSWER: It is difficult to imagine that OCDD could harm human health unless a person were to eat a large amount of it (greater than 1/10 to 1/2 pound of pure OCDD at one time based on animal data). There were no toxic effects noted in the studies sufficient to predict any specific effects for humans. OCDD is no more toxic than a great many other chemicals considered to be low in toxicity and has produced no outstanding effects which would call it to the attention of toxicologists, were it not for its name and structure.

References

(1) Schwetz, B.A., et al. Toxicology of Chlorinated Dibenzo-p-dioxins. Environmental Health Perspectives. 4: 87-99, 1973.

(2) Leng, Marguerite L. Comparative Toxicology of Various Chlorinated Dioxins as Related to Chemical Structure. (Presented at symposium of Collaborative International Pesticide Analytical Council (CIPAC) Baltimore, Maryland, June 7, 1979).

(3) Kociba, R. J. and Schwetz, B.A. A Review of the Toxicity of 2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD) with a comparison to the Toxicity of Other Chlorinated Dioxin Isomers. Association of Food and Drug Officials Quarterly Bulletin. 46(3): 168-188, 1982.

DIOXIN IN THE AIR

4. An earlier draft of the "Trace Chemistries of Fire" was submitted to EPA by Dow Chemical Company in a letter of June 28, 1978. The draft contained data that Dow had detected levels of dioxin ranging up to 8,200 ppb in fly ash particulates from the rotary kiln stack when used without supplemental fuel.

A. Is the Dow rotary incinerator currently operated either with or without the use of supplemental fuel?

ANSWER: It is operated with supplemental fuel to provide more uniform temperature and to increase efficiency and capacity.

B. When was the operation without supplemental fuel discontinued?

ANSWER: The use of supplemental fuel was increased at least 400% as of approximately September 1978.

C. For how long was the rotary kiln incinerator operated without the use of supplemental fuel?

ANSWER: The current incinerator was started up in 1974 with lower amounts of supplemental fuel. An earlier incinerator was operated from approximately 1958 until approximately 1975 without supplemental fuel.

D. What were the levels of dioxin emitted during the operation of the rotary incinerator?

ANSWER: Refer to question and answer 2.E.

E. Was dioxin present in the chemicals or materials before they were burned in the incinerator?

ANSWER: We would expect so in some cases. Please refer to question and answer 2.E.

F. Has the level of dioxin contamination in the chemicals burned in the incinerator ever been tested?

ANSWER: Please refer to question and answer 2.E.

G. Would you object to EPA monitoring the exhaust from the incinerator for dioxin? If so why?

ANSWER: No. In fact, testing was done last fall in conjunction with the Michigan Department of Natural Resources, with whom the results have been shared.

H. Does the Dow plant presently emit dioxin into the atmosphere from any source? If so, at what levels?

ANSWER: One of the initiatives described in the June 1, 1983 announcement referred to in question and answer 2.D. above is a point source investigation of sources of dioxin inside the Midland plant which will be audited by independent scientists. That investigation will include a review of information which will be responsive to the question and the results will be shared with the Environmental Protection Agency and Michigan Department of Natural Resources. Please see Exhibit B for further information.

DOW STUDY OF WIVES OF PLANT WORKERS

5. An article published in the January 5, 1981 issue of Chemical and Engineering News was titled ""Dow Study Finds 2,4,5-T no Pregnancy Risk." The article, which was not peer reviewed, concluded that no significant differences in miscarriages, stillbirths, infant deaths, or malformations were noted between wives of 2,4,5-T workers and unexposed workers.

NOTE: The following information was supplied by Dow's Health & Environmental Sciences Department.

A. We have not seen the original study; would you please send us a copy?

ANSWER: We are surprised that you have not seen a copy since one was attached to Dr. Gehring's March 23, 1983 testimony as one of numerous exhibits. We are concerned that this may indicate you have none of the other exhibits, either. If this is the case, please advise us so we can furnish an additional set. An additional copy of the above-cited study and another article referring to it are enclosed as Exhibits C & D.

B. Did the study include wives and employees who worked at the Dow plant in Midland during the period of 1970 and 1975?

ANSWER: The study considered the reproductive history of wives of employees, both exposed and controls, who worked at Dow between January 1939 and December 1975.

C. Did the unexposed workers also work at the Dow plant in Midland during the period of 1970 and 1975?

ANSWER: Yes, see answer to part B above.

D. Did the study indicate the levels of dioxin that the 2,4,5-T workers were exposed to?

ANSWER: As you will see from the copy of the study enclosed, dioxin levels were addressed in a qualitative sense, with each job being assigned an exposure potential.

E. A summary of this study was eliminated from the final draft of "A Report on Polychlorinated Dibenzo-p-dioxins (PCDDs) and Polychlorinated Dibenzofurans (PCDFs): A Summary of Studies Conducted in the Great Lakes Area," by EPA. Did Dow request that the Dow study be removed from the EPA report? If so why?

ANSWER: No.

SOURCE OF DIOXIN IN DOW OUTFLOW

6. Does the Dow plant in Midland, Michigan currently manufacture 2,4,5-T?

ANSWER: No.

7. Dioxin has been detected in the water that Dow released into the Tittabawassee River and in fish living below the Dow outflow. What is the source of the dioxin that comes from the Dow plant? Are the water treatment facilities at the Dow plant in Midland, Michign contaminated with dioxin?

ANSWER: Information responsive to these questions is being addressed in the point source study referred to in question and answer 4.H. Please refer to Exhibit B for further information.

RESPONSE TO THE MAY 25, 1983, QUESTIONS OF THE SUBCOMMITTEE ON NATURAL RESOURCES, AGRICULTURE RESEARCH AND ENVIRONMENT

Prepared by Region V Staff
United States Environmental Protection Agency

Question

1. The May 1981 draft of a review of dioxin sources and effects by Dr. Milton Clark contained several sections relating to the health and environmental effects of dioxin. In the final report most, if not all, of these sections were missing. One entire section relates to a summary of toxicological effects of dioxin in animals.

   A. Would you, or your staff, explain what these studies concluded and indicate, scientifically, how valid the studies are?

   B. Do these studies draw any conclusions on how toxic dioxin is?

Response

The toxicological studies cited on pages 6 and 7 of the second draft of Region V's report on dioxins concluded 2,3,7,8-TCDD (dioxin) to be acutely toxic, chronically toxic, fetotoxic, teratogenic, and carcinogenic. On a molecular basis, 2,3,7,8-TCDD is considered by some scientists to be the most poisonous synthetic chemical. For additional information, see the joint report of the National Institute of Environmental Health Sciences and the International Agency for Research on Cancer published in Environmental Health Perspectives, November 1980.

For any scientific study to be considered conclusive, acceptable protocols, such as the use of controls, must be employed by the researcher. Before studies are accepted for publication in refereed journals, they are reviewed by scientists familiar with the particular area of investigation. Therefore, most studies involving 2,3,7,8-TCDD which appear in scientific journals, including those cited in Region V's draft report, should be valid.

Question

2. Another section eliminated from the final draft was a summary of the toxicological effects of dioxins on humans. This included studies in Missouri and in Alsea, Oregon.

   A. Would you, or your staff, explain what these studies concluded?

B. The Alsea, Oregon, study related to spontaneous abortions that were believed to be caused by spraying of 2,4,5-T contaminated with dioxin. Is there any connection between this study and Midland, Michigan, either in the original study or in the subsequent criticisms, including those made by Dow?

Response

Conclusions from the Missouri and Alsea, Oregon, studies may be found on pages 9 and 10 of the second draft of Region V's report on dioxins. It should be noted that the U.S. Environmental Protection Agency (EPA) is currently reviewing the Alsea study, and preliminary assessments have indicated methodological problems which renders the conclusions of the study unclear. Further discussion of these studies are included in the publication Dioxins, by Esposito, et al., EPA-600-2-80-197, November 1980; the Federal Register, Vol. 43, No. 78, April 21, 1978; and the Federal Register, Vol. 44, No. 52, March 15, 1979.

In Mr. Charles Poole's testimony before the Subcommittee on March 23, 1983, Mr. Poole stated that in response to EPA's Alsea, Oregon, study, Dow Chemical had submitted data from the Midland County hospital to show that seasonal patterns in miscariages, like the one reported in Oregon, can occur in areas where there are no commercial forests. Because Midland has been a site of 2,4,5,-T production and dioxins have been found in soils and in fish at Midland, the use of Midland data as a "control" group to critique the Alsea study would be inappropriate. For additional information and other opinions, you may wish to contact Mr. Charles Poole of Harvard University, Dr. Vernon Houk of the Centers for Disease Control in Atlanta, or Dr. Phillip Landegren of the National Institute of Occupational Safety and Health in Cincinnati, Ohio.

Question

3. The section that EPA had concluded widespread environmental contamination by dioxin existed and this represented a substantial risk, was also removed. This conclusion was followed by a statement the "EPA also concluded that Dow's discharge represented the major source, if not the only source of TCDD (dioxin) contamination found in the Tittabawassee and Saginaw Rivers and Saginaw Bay in Michigan."

   A. On what evidence were these conclusions based?

   B. Scientifically, how valid were these conclusions?

   C. Since this report was published in July 1981 do you have any additional evidence that Dow is still contaminating the river?

Response

In August 1978, EPA personnel in the Assessment Division in Washington evaluated the results of Dow Chemical's environmental monitoring study. Dow reported finding TCDD: (1) only in caged fish placed in its tertiary pond effluent and not in fish placed upstream of the discharge or in control fish, (2) in caged fish placed 6 miles downstream of Dow's outfall, and (3) in native catfish samples collected from the Tittabawassee River and Saginaw Bay. Based upon this data, EPA formed a preliminary conclusion that a substantial risk of injury to human health or the environment existed, as defined under section 8(e) of the Toxic Sustances Control Act ("widespread and previously unsuspected distribution in environmental media").

The Dow Chemical caged fish study also supported EPA's 1978 conclusion that "Dow's discharge represents the major source, if not the only source, of TCDD contamination found in the Tittabawassee and Saginaw Rivers and Saginaw Bay in Michigan." EPA maintained this conclusion following Dow's November 15, 1978, submission of Trace Chemistries of Fire, where Dow reported finding high concentrations of polychlorinated dibenzodioxins (PCDDs) in soils in Midland. The data indicated that the highest reported concentrations of PCDDs and that of 2,3,7,8-TCDD were considerably greater at Midland than at other locations in the country. EPA speculated that the formation of PCDDs from combustion processes was most likely due to the burning of materials by Dow Chemical already containing PCDDs or PCDD precursors (polychlorophenoxy material).

No other evidence other than weakly circumstantial data has been submitted by Dow Chemical or discovered by U.S. Environmental Protection Agency to refute or significantly modify these conclusions reached in 1979. We, therefore, believe these conclusions to be essentially valid from a scientific point of view. A more complete description and evaluation of data upon which these conclusions are based can be found in the following memorandums which were provided to Dr. Jim Greene of your staff:

1. August 8, 1978, communication to Joseph J. Merenda, Director, Assessment Division, OTE/OTS, "Interim Status Report 8EHQ-0778-0209," from Frank J. Kover, OTE/OTS.

2. September 6, 1978, communication to Ethyl H. Blair, Dow Chemical, "EPA Document Control No. 83HQ-0778-0209," from Warren R. Muir, OTS, EPA.

3. February 8, 1979, communication to Joseph J. Merenda, Director, Assessment Division, OTE/OTS, "Status Report (Supplement) 8EHQ-1178-0209," from Frank D. Kover, OTE/OTS.

The bioaccumulation study conducted by U.S. Environmental Protection Agency in 1981 and published March 28, 1983 (Dow Chemical Company - Midland Plant Wastewater Characterization Study; Preliminary Summary of Results), provides more recent and highly conclusive evidence that dioxins and dibenzofurans were being discharged into the Tittabawassee River.

Question

4. Another section removed contained a study of Dow chemical wives of 2,4,5-T workers. This study was done by Dow.

   A. Why was this section eliminated?

   B. Was the scientific validity of the study questionable?

   C. What were the strengths and weaknesses of this Dow study?

Response

The section describing the Dow Chemical study (Townsend, et al., Amer. J. of Epidem., 115(5), 1982) of wives of 2,4,5-T workers was removed per the instructions EPA personnel in Headquarters. The authors of the Dow reproductive study reported that no unfavorable reproductive effects could be found in wives whose husbands had been exposed to 2,3,7,8-TCDD or other dioxins. The study compared the reproductive outcomes of a control group of Midland wives whose husbands had worked at the Dow facility in Midland, but not with chemicals containing dioxins, with a group of wives whose husbands had worked with dioxin-contaminated chemicals. For an unknown reason, the difference in conceptions between these two groups, which was substantial (2,031 for the control group, 737 for the exposed group), was not analyzed by the authors. The difference is of such magnitude to suggest that exposure to dioxins could have affected male fertility. This observation should be further explored.

The study may also have a second significant weakness in that no true control population or a group unexposed to dioxins exists in Midland. Therefore, differences in many reproductive parameters might not be discerned, as found in the Dow study. Statistical comparisons should have been made with worker populations not having chemical exposure and with State and National reproductive rates.

The authors of the study also did not evaluate the reproductive outcomes for specific time periods, such as the years 1971 to 1974. This time period or 1970-1975 has been shown to contain a statistically significant increase in the rates of cleft lip and cleft palate birth defects in Midland County when compared to overall State rates. Mr. Charles Poole studied the Dow reproductive data (see March 23, 1983, testimony before the Subcommittee) for the 1971-1974 time period and found an apparent significant association with worker exposure to dioxins at the Dow facility in Midland and cleft lip and cleft palate birth defects in their children. Mr. Poole has recommended, and we would concur, that a case control study on Dow workers exposed to dioxins is needed to draw more definitive conclusions that exposure to dioxins in Midland may be responsible for the observed increases in birth defects.

For additional opinions, we suggest you contact those individuals listed in the response to question number 2.

Question

5. EPA recently concluded a study of the Tittabawassee River which flows by the Dow plant in Midland, Michigan. The results of bioaccumulation studies indicate that fish kept in cages below the Dow discharge contained dioxin at a level of 100 parts per trillion (ppt). This is twice maximum the level that the Food and Drug Administration has set for edible portions of fish (50 ppt).

   A. Briefly describe these tests and indicate how valid they are scientifically.

   B. Did you test fish above and below the Dow plant? If so, what were the results of the tests above the Dow plant?

   C. Does this mean that the Dow plant in Midland is still releasing dioxin into the river? Could there be another source of the dioxin other than the Dow Chemical plant?

Response

The caged fish study was designed to determine whether bioaccumulating substances of environmental concern, particularly chlorinated dioxins and dibenzofurans, were being discharged from Dow's Midland plant to the Tittabawassee River. Fish were held for 28 days in cages in the River upstream and downstream of Dow's wastewater outfalls. One of the cages was positioned immediately below the main process discharge, outfall 031, where the wastewater was mixing with the River (estimated dilution of 1:1).

Owing to resource limitations, analysis of the fish was done in stages. So far we have results for fish held 28 days at the location closest to the 031 outfall and at two locations upstream of the plant. These results unequivocally demonstrate that the Dow plant was discharging, at the time of the study in September 1981, levels of chlorinated dioxins sufficient to bioaccumulate in fish to concentrations of concern. Fish held upstream of the plant showed either no detectible chlorinated dioxin or only trace levels (less than 10 parts per trillion).

The data released so far are considered by EPA to be valid, based upon the extensive quality control work performed to date. Further quality control and method validation efforts are included in the work now underway to complete all outstanding analyses of fish and other samples. All of the results will be presented in the final report on the study, which will be available by late summer of this year.

EPA is not aware of any data more recent than September 1981 on the level of dioxins in Dow's discharges. Neither does EPA know of any data or other evidence indicating the presence of another source of dioxin to the Tittabawassee/Saginaw River basin.

For additional information on the bioaccumulation study, please see the March 28, 1983, Dow Chemical Company - Midland Plant Wastewater Characterization Study: Preliminary Summary of Results, by Eastern District Office, Region V, U.S. Environmental Protection Agency, specifically pages 32 to 43 and Appendix E.

Questions For

Valdas V. Adamkus

SECTIONS ELIMINATED FROM DIOXIN SUMMARY DRAFT

1. The May 1981 draft of a review of dioxin sources and effects by Dr. Milton Clark contained several sections relating to the health and environmental effects of dioxin. In the final report most, if not all, of these sections were missing. One entire section relates to a summary of toxicological effects of dioxin in animals.
    A. Would you, or your staff, explain what these studies concluded and indicate, scientifically, how valid the studies are?
    B. Do these studies draw any conclusions on how toxic dioxin is?

2. Another section eliminated from the final draft was a summary of the toxicological effects of dioxins on humans. This included studies in Missouri and in Alsea, Oregon.
    A. Would you, or your staff, explain what these studies concluded?
    B. The Alsea, Oregon study related to spontaneous abortions that were believed to be caused by spraying of 2,4,5-T contaminated with dioxin. Is there any connection between this study and Midland, Michigan either in the original study or in the subsequent criticisms, including those made by Dow?

3. The section that EPA had concluded widespread environmental

RESPONSES BY DR. VERNON HOUK, CENTERS FOR DISEASE CONTROL, TO QUESTIONS FROM MR. JAMES SCHEUER, CHAIRMAN, SUBCOMMITTEE ON NATURAL RESOURCES, AGRICULTURE RESEARCH AND ENVIRONMENT

1. Question: Are you familiar with the increase in birth defects in Midland, Michigan, from 1970-1975?

Answer: Answered at the hearing: Page 117, paragraph 2: "CDC first learned of a possible increase . . . ."

2A. Question: On a nationwide basis, do such increases occur often?

Answer: If you analyze any 1 year of data from the Birth Defects Monitoring Program for statistically significant increases in any of the 150 birth defect categories in any of the 750 reporting counties, you would typically identify about 2,000 increases in birth defects over expected levels.

2B. Question: What are some of the causes for such increases?

Answer: A number of followup studies have been conducted over the years. The results of a majority of these studies suggest that these increases may be due to artifactual reasons such as variable diagnosis and miscoding of diagnosis. These followup investigations have not found a causal association between birth defects and etiologic agents. Discovering the causes of birth defects is difficult. Some of these increases may be due to individual environmental exposures.

3A. Question: What could be the causes of such an increase in Midland? Could dioxin in the environment be a cause?

Answer: The increase in birth defects in Midland was predominately in minor defect categories, which could have been caused by better reporting. One defect category of particular concern was the increase of total oralfacial clefts. Cleft lip with or without cleft palate and cleft palate alone as categories of birth defects are quite heterogeneous with regard to etiology. Many genetic and environmental factors may cause these birth defects, and one or more of these etiologic factors could have caused the increase in Midland. It is possible that the increase in birth defects was caused by dioxin, but there is no evidence that it did.

We should underscore the fact that a statistically significant increase may occur by chance alone.

3B. Question: What studies should be undertaken to determine the causes of the increase in birth defects in Midland?

Answer: Answered at the hearing, page 125: "DR. HOUK. I don't recommend a specific study . . . ."

4. Question: Do you have accurate data on the rate of birth defects in Midland from 1960 to the present? If so, what does the data indicate, if anything?

Answer: We do not have data on the rate of birth defects in Midland from 1960. Our Birth Defects Monitoring Program was initiated in 1974 with the purchase of existing data back to 1970.

5. Question: We have been talking with some of the wives of Dow employees in Midland and a high percentage have experienced some type of reproductive disorder. Does this type of information indicate a trend that should be investigated further?

Answer: There are a number of questions which must be answered before we could interpret this information, such as: How were these wives selected? Were the outcomes confirmed? What specific outcomes were reported? How many pregnancies/conceptions have these women experienced? The interpretation of this information is further complicated by the fact that adverse pregnancy outcomes are fairly common. For example, failure to conceive occurs in 10 to 15 percent of couples after 1 year of unprotected intercourse; miscarriages occur in 16 to 20 percent of pregnancies 8 to 28 weeks of gestation; stillbirths occur in 2 to 4 percent of all births; and birth defects occur in 3 to 5 percent of all births. Therefore, in any group of women who have experienced several pregnancies each, we would not be surprised to find some reproductive disorders.

5B. Question: If the Subcommittee staff provides you with a list of wives from Midland who have experienced reproductive disorders, including birth defects, will the Center follow up to determine the validity of the information?

Answer: Within available resources, CDC is willing to follow up information on reproductive disorders including birth defects among Midland wives which this Subcommittee's staff wishes to provide. However, to determine the validity of this information, necessary data must be collected under strict epidemiologic methods and with the full support, cooperation, and participation of the Michigan Department of Health and the Dow Chemical Company.

Responses to "Questions for Mr. Poole"

1.A. The data were generated by the Michigan Department of Public Health (MDPH).

B. I trust that the data are a fairly accurate reflection of the recording of birth defects on certificates of live birth during the years in question. The accuracy of birth certificates as a source of information on the actual frequency of birth defects, however, is questionable. In general, birth certificates are believed to provide underestimates of the actual number of birth defects.

C. Dr. Richard Hill of the staff of the Assistant Administrator for Pesticides and Toxic Substances at EPA first told me of the existence of the data. I subsequently obtained data on the subject from the published literature, the MDPH, and the Dow Chemical Company. (The data from Dow Chemical, originally produced by the MDPH, were introduced as cross-examination exhibits at a hearing in which I testified shortly after the EPA suspension of certain uses of 2,4,5-T in 1979.)

2.A. See response to Question 1.A.

B. See response to Question 1.B.

C. I believe that the case-control study I designed would be a good approach toward discovering the reason or reasons for the transiently elevated appearance of birth defects on birth certificates in Midland County during the early 1970's.

3.A. I have no doubt that Dr. Rice's statement was valid in the sense that it accurately represented his opinion on the matter. I would not be in a position to offer an informed opinion until I had the opportunity to examine the results of a more in-depth investigation, such as the one I have suggested.

B. There are many possible explanations. They fall into three categories: increased diagnostic awareness, increased reporting of diagnoses, and temporal modulation of risk factors.

C. I do not find the segregation of birth defects into the categories "minor" and "major" to be particularly useful from an epidemiologic perspective. It is doubtful that the causes of birth defects would be aligned according to such categories. Congenital anomalies that do not threaten life or interfere with physical or social development might be considered minor, but it would be worthwhile still to direct epidemiologic research toward elucidation of their causes.

D. The data drom the Dow Chemical study of reproductive histories of wives of workers potentially exposed to polychlorinated dibenzodioxins (PCDD) are relevant to the questions of increased occurrence versus increased diagnosis versus increased reporting. My analysis of those data tends to support increased diagnosis or occurrence, rather than increased reporting. The reason is that the recall of mothers should have little to do with the recording of malformations on birth certificates.

Midland County data on late fetal mortality also are relevant. As late fetal mortality rates did not fall concomitantly with the rise in birth defect rates, it is likely that the apparent increase was not caused by a change in recording practices with respect to deaths occurring very close to parturition (i.e., the use of a certificate of live birth followed closely by a standard certificate of death versus the use of a certificate of fetal death).

E. Whether the increase occurred because of a change in diagnosis, reporting, or risk factors, the change would have to have been abrupt and temporary -- its effect beginning in 1970 or 1971 and ending in 1974 or 1975.

4.A. At the time of drafting the original proposal in 1979, I was under the impression that cleft lip and palate had been the major findings in the laboratory studies. I since have learned that a wide variety of teratogenic effects have been produced. As I am not a toxicologist and as interspecies discordance is not uncommon, I now would refrain from placing great stock in comparisons of epidemiologic and toxicologic findings in different species.

B. The only other evidence of which I am aware is the data from the Dow Chemical study to which I have referred. My analysis tended to suggest that direct, potential, paternal exposure to PCDD either did not produce birth defects in Midland County during this period of time or produced a very small fraction of the apparent overall excess.

C. Environmental exposures, broadly defined, are always among the factors suspected to be the cause of any temporary increase in disease frequency.

D. Heredity and artifact (i.e., of diagnostic or reporting practices) are the other categories of possible explanations. I would assign heredity a low degree of credence because of the sharpness of the increase and subsequent decrease over such a short period of time.

E. "Proof," in an absolute sense, is never achieved. The study I have proposed is the best one I could devise to evaluate this and other hypotheses.

5.A. No.

B. See response to Question 4.B.

6. It is difficult for me to recall at this point all the people who received copies of my 1979 proposal. I am sure that I gave it or showed it to people in various parts of the Office of Toxic Substances and the Office of General Counsel of EPA, the CDC, and the MDPH.

7. My direct supervisors at EPA took no action with respect to my proposal, which was never formally submitted because of the necessity of first obtaining cooperation from Dow Chemical. My supervisors neither supported nor suppressed the idea. The Office of General Counsel kept abreast of my plans to develop the study and advised me

with respect to contacting Dow Chemical. The CDC expressed approval of the scientific merit of the project and offered assistance in securing the necessary institutional arrangements, especially with the MDPH. Staff at the MDPH expressed a willingness to cooperate with the study.

8. To my knowledge, no one at EPA or elsewhere conducted research to evaluate the apparent 1971-74 excess.

Charles Poole

Charles Poole
August 1, 1983